28 July 2021
EMA/CHMP/294837/2021 Corr.1[1]
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Minutes for the meeting on 19-22 April 2021

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

Disclaimers

Some of the information contained in this set of minutes is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also vary during the course of the review. Additional details on some of these procedures will be published in the CHMP meeting highlights once the procedures are finalised and start of referrals will also be available.

Of note, these minutes are a working document primarily designed for CHMP members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

[1] Correction in section 8.1.1

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Table of contents

1. Introduction 7

1.1. Welcome and declarations of interest of members, alternates and experts 7

1.2. Adoption of agenda 7

1.3. Adoption of the minutes 7

2. Oral Explanations 8

2.1. Pre-authorisation procedure oral explanations 8

2.1.1. Evkeeza - evinacumab - EMEA/H/C/005449 8

2.2. Re-examination procedure oral explanations 8

2.3. Post-authorisation procedure oral explanations 8

2.4. Referral procedure oral explanations 8

3. Initial applications 8

3.1. Initial applications; Opinions 8

3.1.1. Abiraterone KRKA - abiraterone acetate - EMEA/H/C/005649 8

3.1.2. Adtralza - tralokinumab - EMEA/H/C/005255 9

3.1.3. Celsunax - ioflupane (^{123}I) - EMEA/H/C/005135 9

3.1.4. Enspryng - satralizumab - Orphan - EMEA/H/C/004788 10

3.1.5. Evkeeza - evinacumab - EMEA/H/C/005449 10

3.1.6. Jayempi - azathioprine - EMEA/H/C/005055 11

3.1.7. Koselugo - selumetinib - Orphan - EMEA/H/C/005244 12

3.1.8. Onureg - azacitidine - EMEA/H/C/004761 12

3.2. Initial applications; List of outstanding issues (Day 180; Day 120 for procedures with accelerated assessment timetable) 13

3.2.1. abiraterone acetate - EMEA/H/C/005368 13

3.2.2. bimekizumab - EMEA/H/C/005316 13

3.2.3. lisocabtagene maraleucel - Orphan - ATMP - EMEA/H/C/004731 13

3.2.4. zanubrutinib - Orphan - EMEA/H/C/004978 13

3.2.5. odevixibat - Orphan - EMEA/H/C/004691 14

3.2.6. pralsetinib - EMEA/H/C/005413 14

3.2.7. imatinib - EMEA/H/C/005595 14

3.2.8. tirbanibulin mesilate - EMEA/H/C/005183 15

3.2.9. pitolisant - EMEA/H/C/005117 15

3.2.10. eladocagene exuparvovec - Orphan - ATMP - EMEA/H/C/005352 15

3.2.11. elivaldogene autotemcel - Orphan - ATMP - EMEA/H/C/003690 16

3.2.12. vosoritide - Orphan - EMEA/H/C/005475 16

3.3. Initial applications; List of questions (Day 120; Day 90 for procedures with accelerated assessment timetable) 16

3.3.1. betaine anhydrous - EMEA/H/C/005637 16
3.3.2. artesunate - Orphan - EMEA/H/C/005718 16
3.3.3. hepatitis B surface antigen - EMEA/H/C/005466 17
3.3.4. pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477 17
3.3.5. bevacizumab - EMEA/H/C/005574 17
3.3.6. inebilizumab - Orphan - EMEA/H/C/005818 18
3.3.7. vildagliptin / metformin hydrochloride - EMEA/H/C/005738 18
3.3.8. diroximel fumarate - EMEA/H/C/005437 18
3.3.9. eptinezumab - EMEA/H/C/005287 18
3.3.10. linzagolix choline - EMEA/H/C/005442 18
3.4. Update on on-going initial applications for Centralised procedure 19
3.4.1. doxorubicin hydrochloride - EMEA/H/C/005330 19
3.4.2. adalimumab – EMEA/H/C/005548 19
3.4.3. maralixibat - Orphan - EMEA/H/C/005551 19
3.4.4. rivaroxaban - EMEA/H/C/005600 20
3.4.5. sildenafil - EMEA/H/C/005439 20
3.5. Re-examination of initial application procedures under Article 9(2) of Regulation no 726/2004 20
3.5.1. Aplidin - plitidepsin - Orphan - EMEA/H/C/004354 20
3.6. Initial applications in the decision-making phase 20
3.7. Withdrawals of initial marketing authorisation application 21

4. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008 21

4.1. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinion 21
4.1.1. Aubagio - teriflunomide - EMEA/H/C/002514/X/0031/G 21
4.1.2. Fabrazyme - agalsidase beta - EMEA/H/C/000370/X/0118/G 21
4.1.3. Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/X/0033/G 22
4.2. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 list of outstanding issues 22
4.2.1. Pheburane - sodium phenylbutyrate - EMEA/H/C/002500/X/0026 22
4.2.2. Pheburane - sodium phenylbutyrate - EMEA/H/C/002500/X/0028 23
4.3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 120 List of question 23
4.3.1. Adynovi - rurioctocog alfa pegol - EMEA/H/C/004195/X/0018 23
4.3.2. Paliperidone Janssen-Cilag International - paliperidone - EMEA/H/C/005486/X/0002/G 24
4.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008 24
4.4.1. Lacosamide Accord - lacosamide - EMEA/H/C/004443/X/0007 24

4.5. Re-examination procedure of extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008 25

5. Type II variations - variation of therapeutic indication procedure according to Annex I of Commission Regulation (EC) No 1234/2008 25

5.1. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information 25

5.1.1. BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/II/0033/G 25

5.1.2. Crysvita - burosumab - Orphan - EMEA/H/C/004275/II/0023 26

5.1.3. DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/II/0033/G 26

5.1.4. Esbriet - pirfenidone - EMEA/H/C/002154/II/0069 27

5.1.5. Jardiance - empagliflozin - EMEA/H/C/002677/II/0055 27

5.1.6. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0097 28

5.1.7. Nulojix - belatacept - EMEA/H/C/002098/II/0070 28

5.1.8. Tagrisso - osimertinib - EMEA/H/C/004124/II/0039/G 29

5.1.9. Ultomiris - ravulizumab - EMEA/H/C/004954/II/0010 29

5.1.10. Venclyxto - venetoclax - EMEA/H/C/004106/II/0030 29

5.1.11. WS1881 Opdivo - nivolumab - EMEA/H/C/003985/WS1881/0091 Yervoy - ipilimumab - EMEA/H/C/002213/WS1881/0085 30

5.1.12. WS1952 Edistride - dapagliflozin - EMEA/H/C/004161/WS1952/0042 Forxiga - dapagliflozin - EMEA/H/C/002322/WS1952/0060 30

5.2. Update on on-going Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008 31

5.2.1. Brilique - ticagrelor - EMEA/H/C/001241/II/0047/G 31

5.3. Re-examination of Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008 31

6. Ancillary medicinal substances in medical devices 31

6.1. Ancillary medicinal substances in medical devices; Opinions/ Day 180 list of outstanding issues / Day 120 list of questions 31

6.2. Update of Ancillary medicinal substances in medical devices 32

7. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use) 32

7.1. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)32

8. Pre-submission issues 32

8.1. Pre-submission issue 32

8.1.1. copanlisib – H0004334 32

8.1.2. budesonide – H0005653 32

8.1.3. maribavir - Orphan - H0005787 32

8.2. Priority Medicines (PRIME) 33

8.2.1. List of applications received 33
8.2.2. Recommendation for PRIME eligibility 33

9. Post-authorisation issues 33

9.1. Post-authorisation issues 33
9.1.1. Veklury – remdesivir - EMEA/H/C/005622/LEG/031 33
9.1.2. Veklury - remdesivir - EMEA/H/C/005622/R/0015 33
9.1.3. Invokana - canagliflozin - EMEA/H/C/002649/II/0055 34
9.1.4. Iscover-EMEA/H/C/000175/WS1820/0142 Plavix-EMEA/H/C/000174/WS1820/0140 34
9.1.5. COVID-19 Vaccine Janssen – COVID-19 vaccine (Ad26.COV2-S [recombinant]) – EMEA/H/C/005737 34
9.1.6. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0102 35
9.1.7. Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/ANX/001.6 35
9.1.8. VITRAKVI - larotrectinib - EMEA/H/C/004919/II/0010/G 35

10. Referral procedures 36

10.1. Procedure for Centrally Authorised products under Article 20 of Regulation (EC) No 726/2004 36
10.2. Requests for CHMP Opinion under Article 5(3) of Regulation (EC) No 726/2004 . 36
10.2.1. Vaxzevria – COVID-19 Vaccine (ChAdOx1-S [recombinant]) – EMEA/H/A-5(3)/1507 36
10.2.2. GSK4182136 (VIR-7831) for the treatment of COVID-19 - EMEA/H/A-5(3)/1508 37
10.3. Procedure under Articles 5(2) and 10 of Regulation (EC) No 726/2004 37
10.4. Disagreement between Member States on application for medicinal product (potential serious risk to public health) –under Article 29(4) of Directive 2001/83/EC 37
10.5. Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC.... 37
10.6. Community Interests - Referral under Article 31 of Directive 2001/83/EC 37
10.7. Re-examination Procedure under Article 32(4) of Directive 2001/83/EC..... 38
10.8. Procedure under Article 107(2) of Directive 2001/83/EC 38
10.9. Disagreement between Member States on Type II variation– Arbitration procedure initiated by MAH under Article 6(13) of Commission Regulation (EC) No 1084/2003 38
10.10. Procedure under Article 29 of Regulation (EC) 1901/2006..... 38
10.11. Referral under Article 13 Disagreement between Member States on Type II variation– Arbitration procedure initiated by Member State under Article 13 (EC) of Commission Regulation No 1234/2008 38

11. Pharmacovigilance issue 38

11.1. Early Notification System 38

12. Inspections 38

12.1. GMP inspections 38

12.2. GCP inspections 38
12.3. Pharmacovigilance inspections 39
12.4. GLP inspections 39

13. Innovation Task Force 39
13.1. Minutes of Innovation Task Force 39
13.2. Innovation Task Force briefing meetings 39
13.3. Requests for CHMP Opinion under Article 57(1)J and (1)P of Regulation (EC) No 726/2004 39
13.4. Nanomedicines activities 39

14. Organisational, regulatory and methodological matters 39
14.1. Mandate and organisation of the CHMP 39
14.1.1. Resourcing of Covid-19 applications: Follow up from February and March CHMP meetings 39
14.2. Coordination with EMA Scientific Committees 40
14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC) 40
14.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups 40
14.3.1. Biologics Working Party (BWP) 40
14.3.2. Name Review Group (NRG) 40
14.3.3. Safety Working Party (SWP) 40
14.3.4. Pharmacokinetics Working Party (PKWP) 41
14.3.5. Scientific Advice Working Party (SAWP) 41
14.4. Cooperation within the EU regulatory network 41
14.5. Cooperation with International Regulators 41
14.6. Contacts of the CHMP with external parties and interaction with the Interested Parties to the Committee 41
14.7. CHMP work plan 41
14.8. Planning and reporting 41
14.9. Others 42

15. Any other business 42
15.1. AOB topic 42
15.1.1. Update on COVID-19 42
15.1.2. COVID-19 mRNA vaccine - EMEA/H/C/005845 42

Lists of participants 43
Explanatory notes 53

1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts

The Chairperson opened the meeting by welcoming all participants. Due to the current coronavirus (COVID-19) outbreak, and the associated EMA Business Continuity Plan (BCP), the meeting was held remotely.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions. See April 2021 CHMP minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session held 19 – 22 April 2021.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 17 or more members were present remotely). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

CHMP agenda for 19-22 April 2021

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 22-25 March 2021

Minutes from PRocedural and Organisational Matters (PROM) meeting held on 12 April 2021

The CHMP adopted the CHMP minutes for 22-25 March 2021.

The CHMP adopted the minutes from the PROM meeting held on 12 April 2021.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. Evkeeza - evinacumab - EMEA/H/C/005449

Regeneron Ireland Designated Activity Company (DAC); treatment of homozygous familial hypercholesterolemia (HoFH)

Scope: Oral explanation

Action: Oral explanation to be held on Tuesday, 20 April 2021 at 14:00

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 25.03.2021, 23.02.2021. List of Questions adopted on 08.12.2020.

An oral explanation was held on Tuesday, 20 April 2021. The presentation by the applicant mainly focused on the specific obligations in light of a marketing authorisation under exceptional circumstances.

See 3.1

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Abiraterone KRKA - abiraterone acetate - EMEA/H/C/005649

KRKA, d.d., Novo mesto; treatment of prostate cancer in adult men

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Zytiga

List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 12.11.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.1.2. Adtralza - tralokinumab - EMEA/H/C/005255

LEO Pharma A/S; treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy

Scope: Opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 17.09.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that tralokinumab is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendation dated 21 April 2021.

The summary of opinion was circulated for information.

3.1.3. Celsunax - ioflupane (^{123}I) - EMEA/H/C/005135

Pinax Pharma GmbH; indicated for detecting loss of functional dopaminergic neuron terminals in the striatum

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of DaTSCAN

List of Outstanding Issues adopted on 25.02.2021, 15.10.2020. List of Questions adopted

on 14.11.2019.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendation dated 19.04.2021.

The summary of opinion was circulated for information.

3.1.4. Enspryng - satralizumab - Orphan - EMEA/H/C/004788

Roche Registration GmbH; treatment of adult and adolescent patients from 12 years of age with neuromyelitis optica spectrum disorders (NMOSD)

Scope: Opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 25.02.2021, 28.05.2020. List of Questions adopted on 10.12.2019.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (25 out of 29) together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that satralizumab is a new active substance, as claimed by the applicant

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The divergent position (Christian Gartner, Maria Concepcion Prieto Yerro, Dana Gabriela Marin, Andrea Laslop) was appended to the opinion.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

3.1.5. Evkeeza - evinacumab - EMEA/H/C/005449

Regeneron Ireland Designated Activity Company (DAC); treatment of homozygous familial hypercholesterolemia (HoFH)

Scope: Oral explanation/opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 25.03.2021, 23.02.2021. List of Questions adopted on 08.12.2020.

See 2.1

An oral explanation was held on Tuesday, 20 April 2021. The presentation by the applicant mainly focused on the specific obligations in light of a marketing authorisation under exceptional circumstances.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation under exceptional circumstances by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that evinacumab is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendation dated 21 April 2021.

The summary of opinion was circulated for information.

3.1.6. Jayempi - azathioprine - EMEA/H/C/005055

Nova Laboratories Ireland Limited; indicated for the prophylaxis of transplant rejection, used as an immunosuppressant antimetabolite, chronic inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis), relapsing multiple sclerosis, generalised myasthenia gravis

Scope: Opinion

Action: For adoption

Hybrid application (Article 10(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 25.02.2021, 15.10.2020. List of Questions adopted on 30.04.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendation dated 20 April 2021.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

3.1.7. Koselugo - selumetinib - Orphan - EMEA/H/C/005244

AstraZeneca AB; treatment of neurofibromatosis type 1 (NF1)

Scope: Opinion

Action: For adoption

New active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 23.07.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a conditional marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that selumetinib is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendation dated 21 April 2021.

The summary of opinion was circulated for information.

3.1.8. Onureg - azacitidine - EMEA/H/C/004761

Bristol-Myers Squibb Pharma EEIG; treatment for acute myeloid leukaemia

Scope: Opinion

Action: For adoption

Known active substance (Article 8(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 17.09.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendation dated 21 April 2021.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

3.2. Initial applications; List of outstanding issues (Day 180; Day 120 for procedures with accelerated assessment timetable)

3.2.1. abiraterone acetate - EMEA/H/C/005368

treatment of metastatic castration resistant prostate cancer

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 23.07.2020.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

3.2.2. bimekizumab - EMEA/H/C/005316

treatment of plaque psoriasis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 10.12.2020.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.3. lisocabtagene maraleucel - Orphan - ATMP - EMEA/H/C/004731

Bristol-Myers Squibb Pharma EEIG; treatment of large B-cell lymphoma, diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B)

Scope: List of outstanding issues

Action: For information

List of Questions adopted on 06.11.2020.

The Committee was reminded of the status of this application and its remaining outstanding issues. The CHMP was updated on discussions at the CAT.

The Committee endorsed the list of outstanding issues with a specific timetable as adopted by the CAT.

3.2.4. zanubrutinib - Orphan - EMEA/H/C/004978

BeiGene Ireland Ltd; treatment of Waldenström's macroglobulinaemia (WM)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.10.2020.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.5. odevixibat - Orphan - EMEA/H/C/004691

Accelerated assessment

Albireo; treatment of progressive familial intrahepatic cholestasis (PFIC)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 23.02.2021.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.6. pralsetinib - EMEA/H/C/005413

treatment of non-small cell lung cancer (NSCLC)

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 28.01.2021. List of Questions adopted on 17.09.2020.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

The CHMP agreed to consult the SAG Oncology and adopted a list of questions to the experts.

3.2.7. imatinib - EMEA/H/C/005595

treatment of Philadelphia chromosome (bcr-abl) positive (Ph+) chronic myeloid leukaemia (CML), Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL), myelodysplastic/myeloproliferative diseases (MDS/MPD), hypereosinophilic syndrome (HES), eosinophilic leukaemia (CEL), Kit (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST), and unresectable dermatofibrosarcoma protuberans (DFSP)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 12.11.2020.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.8. tirbanibulin mesilate - EMEA/H/C/005183

topical field treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 25.06.2020.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

3.2.9. pitolisant - EMEA/H/C/005117

Treatment of Excessive Daytime Sleepiness (EDS) in patients with Obstructive Sleep Apnoea (OSA)

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 25.03.2021, 10.12.2020. List of Questions adopted on 25.06.2020.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 3rd list of outstanding issues with a specific timetable.

3.2.10. eladocagene exuparvovec - Orphan - ATMP - EMEA/H/C/005352

PTC Therapeutics International Limited; treatment of aromatic L-amino aciddecarboxylase (AADC) deficiency

Scope: List of outstanding issues

Action: For information

List of Questions adopted on 20.05.2020.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The CHMP was updated on discussions at the CAT.

The Committee endorsed the list of outstanding issues with a specific timetable as adopted by the CAT.

The CHMP also endorsed the involvement of a SAG.

3.2.11. elivaldogene autotemcel - Orphan - ATMP - EMEA/H/C/003690

Accelerated assessment

bluebird bio (Netherlands) B.V; treatment of ABCD1 genetic mutation and cerebral adrenoleukodystrophy

Scope: List of outstanding issues

Action: For information

List of Questions adopted on 22.01.2021.

The Committee was reminded of the status of this application and its remaining outstanding issues. The CHMP was updated on discussions at the CAT.

The Committee endorsed the list of outstanding issues with a specific timetable as adopted by the CAT.

3.2.12. vosoritide - Orphan - EMEA/H/C/005475

BioMarin International Limited; Indicated for the treatment of achondroplasia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 10.12.2020.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.3. Initial applications; List of questions (Day 120; Day 90 for procedures with accelerated assessment timetable)

3.3.1. betaine anhydrous - EMEA/H/C/005637

treatment of homocystinuria

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.2. artesunate - Orphan - EMEA/H/C/005718

B And O Pharm; Treatment of severe malaria

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.3. hepatitis B surface antigen - EMEA/H/C/005466

indicated for the prevention of infection caused by all known subtypes of the hepatitis B virus in adults

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.4. pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477

immunisation for the prevention of invasive disease and pneumonia caused by Streptococcus pneumoniae

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.5. bevacizumab - EMEA/H/C/005574

Treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.
First-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer.
First-line treatment of patients with advanced and/or metastatic renal cell cancer.

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions.

3.3.6. inebilizumab - Orphan - EMEA/H/C/005818

Viela Bio; indicated for the treatment of adults with neuromyelitis optica spectrum disorders

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.7. vildagliptin / metformin hydrochloride - EMEA/H/C/005738

treatment of type 2 diabetes mellitus

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.8. diroximel fumarate - EMEA/H/C/005437

treatment of relapsing remitting multiple sclerosis

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.9. eptinezumab - EMEA/H/C/005287

indicated for the prophylaxis of migraine in adults

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.10. linzagolix choline - EMEA/H/C/005442

for the management of heavy menstrual bleeding (HMB) associated with uterine fibroids

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.4. Update on on-going initial applications for Centralised procedure

3.4.1. doxorubicin hydrochloride - EMEA/H/C/005330

treatment of breast cancer, treatment of ovarian cancer, treatment of multiple myeloma, treatment of AIDS related Kaposi's sarcoma.

Scope: Request by the applicant dated 14.04.2021 for an extension to the clock stop to respond to the list of questions adopted in May 2020

Action: For adoption

List of Questions adopted on 28.05.2020.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in May 2020

3.4.2. adalimumab – EMEA/H/C/005548

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn’s disease, paediatric Crohn’s disease, ulcerative colitis, uveitis, paediatric uveitis

Scope: Request by the applicant dated 30 March 2021 for an extension to the clock stop to respond to the list of questions adopted in January 2021

Action: For adoption

List of Questions adopted on 28.01.2021.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in January 2021.

3.4.3. maralixibat - Orphan - EMEA/H/C/005551

FGK Representative Service GmbH; Treatment of Progressive Familial Intrahepatic Cholestasis Type 2

Scope: Request by the applicant dated 15 April 2021 for an extension to the clock stop to respond to the list of questions adopted in March 2021

Action: For adoption

List of questions adopted on 25.03.2021

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in March 2021

3.4.4. rivaroxaban - EMEA/H/C/005600

Prevention of venous thromboembolism in adult patients undergoing elective hip or knee replacement surgery and treatment of deep vein thrombosis and pulmonary embolism as well as prevention of recurrent DVT and PE in adults. Treatment of deep vein thrombosis and pulmonary embolism and prevention of recurrent DVT and PE in adults. Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors.

Scope: Request by the applicant dated 15 April 2021 for an extension to the clock stop to respond to the list of questions adopted in January 2021

Action: For adoption

List of questions adopted on 28.01.2021

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in January 2021.

3.4.5. sildenafil - EMEA/H/C/005439

treatment of erectile dysfunction

Scope: Request by the applicant dated 14 April 2021 for an extension to the clock stop to respond to the list of outstanding issues adopted in March 2021

Action: For adoption

List of Outstanding Issues adopted on 25.03.2021, 10.12.2020. List of Questions adopted on 25.06.2020.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in March 2021.

3.5. Re-examination of initial application procedures under Article 9(2) of Regulation no 726/2004

3.5.1. Aplidin - plitidepsin - Orphan - EMEA/H/C/004354

Pharma Mar, S.A.; treatment of multiple myeloma

Scope: Implementation of Judgement of the General Court in Case-T-594/18, draft timetable

Action: For information

New active substance (Article 8(3) of Directive No 2001/83/EC)

Opinion re-examination adopted on 22.03.2018. Opinion adopted on 14.12.2017

The CHMP noticed the update on the procedure.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

4. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

4.1. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinion

4.1.1. Aubagio - teriflunomide - EMEA/H/C/002514/X/0031/G

Sanofi-Aventis Groupe

Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber

Scope: "Extension of a marketing authorisation for Aubagio to add the new strength, 7 mg film-coated tablet, for use in paediatric patients from 10 years of age and older with relapsing remitting multiple sclerosis (MS).
Extension of indication to include treatment of paediatric patients aged 10 years and older with relapsing remitting multiple sclerosis (MS) for Aubagio. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Annex II, labelling and Package Leaflet are updated in accordance.
The MAH is requesting an extension of the market protection of one additional year in line with the guidance on elements required to support the significant clinical benefit in comparison with existing therapies of a new therapeutic indication in order to benefit from an extended (11-year) marketing protection period. Version 7.0 of the RMP has also been agreed."

Action: For adoption

List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 17.09.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

4.1.2. Fabrazyme - agalsidase beta - EMEA/H/C/000370/X/0118/G

Genzyme Europe BV

Rapporteur: Johann Lodewijk Hillege

Scope: Quality changes

Action: For adoption

List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 17.09.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The CHMP noted the letter of recommendation dated 15.04.2021.

4.1.3. Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/X/0033/G

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension application to introduce a new strength and pharmaceutical form (50/20 mg coated granules in sachet), grouped with a type II extension of indication variation (C.I.6.a) to include the treatment of children from 3 to 12 years of age (weighing at least 45 Kg) for the approved Maviret 100 mg/40 mg film-coated tablets. As a consequence of the extended indication, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated accordingly. Furthermore, the MAH took the opportunity to implement several clarifications and editorial changes and to bring the product information in line with the latest QRD template version 10.2. The RMP (version 8) is updated in accordance."

Action: For adoption

List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 17.09.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

4.2. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 list of outstanding issues

4.2.1. Pheburane - sodium phenylbutyrate - EMEA/H/C/002500/X/0026

Eurocept International B.V.

Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension application to introduce a new pharmaceutical form associated with new strength (350 mg/ml oral solution). The RMP (version 0.1) is updated in accordance."

Action: For adoption

List of Questions adopted on 12.11.2020.

The Committee discussed the issues identified in this application, mainly concerning the bioequivalence data.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of outstanding issues and a specific timetable.

The CHMP agreed to consult the PKWP and adopted a list of questions to this group.

4.2.2. Pheburane - sodium phenylbutyrate - EMEA/H/C/002500/X/0028

Eurocept International B.V.

Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension application to introduce a new pharmaceutical form associated with new strength (500 mg film-coated tablets). The RMP (version 0.1) is updated in accordance."

Action: For adoption

List of Questions adopted on 12.11.2020.

The Committee discussed the issues identified in this application, mainly concerning the bioequivalence data and quality aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of outstanding issues and a specific timetable.

The CHMP agreed to consult the PKWP and adopted a list of questions to this group.

4.3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 120 List of question

4.3.1. Adynovi - rurioctocog alfa pegol - EMEA/H/C/004195/X/0018

Baxalta Innovations GmbH

Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst

Scope: "Extension application to add a new strength of 3000 IU for rurioctocog alfa pegol powder and solvent for solution for injection, for intravenous use.
Furthermore, the MAH took the opportunity to include editorial changes to update the naming convention from BAX855 to rurioctocog alfa pegol throughout the section and removed the reference to Baxalta as well as update table numbering throughout the documents in module 3. Furthermore, change omitted from the dossier following approval of variations EMEA/H/C/004195/IB/0004/G and EMEA/H/C/004195/IB/0015/G were also included."

Action: For adoption

The Committee discussed the issues identified in this application, mainly concerning quality aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

4.3.2. Paliperidone Janssen-Cilag International - paliperidone - EMEA/H/C/005486/X/0002/G

Janssen-Cilag International N.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to introduce two new strengths of 700 mg and 1000 mg prolonged-release suspension for injection, grouped with the following variations:
A.2.a - To change the (invented) name of the medicinal product from Paliperidone Janssen-Cilag International
A.7 -
6 x C.I.7.b. - To delete the 25 mg, 50 mg, 75 mg, 100 mg and 150 mg/100 mg strengths from the Paliperidone Janssen-Cilag marketing authorisation (EU/1/20/1453/001-006)."

Action: For adoption

The Committee discussed the issues identified in this application, mainly concerning clinical aspects and the environmental risk assessment.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

4.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008

4.4.1. Lacosamide Accord - lacosamide - EMEA/H/C/004443/X/0007

Accord Healthcare S.L.U.

Rapporteur: John Joseph Borg, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to introduce a new pharmaceutical form (solution for infusion), a new strength (10 mg/ml) and a new route of administration (intravenous use)."

Request from the MAH for an extension of the clock stop to respond to the list of outstanding issues adopted in November 2020.

Action: For adoption

List of Outstanding Issues adopted on 12.11.2020. List of Questions adopted on 26.03.2020.

The CHMP agreed to the request by the applicant for an extension of the clock stop to respond to the list of outstanding issues adopted in November 2020.

4.5. Re-examination procedure of extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

No items

5. Type II variations - variation of therapeutic indication procedure according to Annex I of Commission Regulation (EC) No 1234/2008

5.1. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information

5.1.1. BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/II/0033/G

Teva Pharma B.V.

Rapporteur: John Joseph Borg, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Anette Kirstine Stark

Scope: "Type II variation – C.I.6.a. - Extension of indication to include adolescents (12 years and older) for the regular treatment of asthma, where use of a combination (inhaled corticosteroid and long-acting β2 adrenoceptor agonist) is appropriate: in patients not adequately controlled with inhaled corticosteroids and "as needed" inhaled short-acting β2 adrenoceptor agonists; or in patients already adequately controlled on both inhaled corticosteroids and long-acting β2 adrenoceptor agonists. The proposed extension to the indication is based upon data from the literature.
As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly.
In addition, the MAH took the opportunity to make an administrative update to the Greek, Islandic, Irish and Maltese local representatives phone numbers in the Package Leaflet.
Furthermore, the PI is brought in line with the latest QRD template version 10.1.
An updated RMP version 3.0 was submitted as part of the application.
Type IB variation - C.I.z other – updates of sections 4.2, 5.1 and 5.2 of the SmPC to update the information on paediatric data and section 4.4 of the SmPC to remove the warning regarding the risk of growth retardation in children and the guidance on how to address this risk as agreed during the assessment of the duplicate Budesonide/Formoterol Teva Pharma B.V. (EMEA/H/C/004882), which was approved in Jan 2020."

Action: For adoption

Request for Supplementary Information adopted on 15.10.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.2. Crysvita - burosumab - Orphan - EMEA/H/C/004275/II/0023

Kyowa Kirin Holdings B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include treatment of FGF23-related hypophosphataemia in tumour-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumours that cannot be curatively resected or localised in patients aged 1 year and over, based on data from two ongoing open-label clinical studies, UX023T-CL201 and KRN23-002, in adults with TIO (144-week data and 88-week data are available, respectively). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet is updated accordingly. An updated RMP version 4.0 has also been submitted. The MAH also applied for one additional year of market protection.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

The Committee discussed the issues identified in this application, mainly concerning clinical aspects.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.3. DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/II/0033/G

Teva Pharma B.V.

Rapporteur: John Joseph Borg, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Anette Kirstine Stark

Scope: "Type II variation – C.I.6.a. - Extension of indication to include adolescents (12 years and older) for the regular treatment of asthma, where use of a combination (inhaled corticosteroid and long-acting β2 adrenoceptor agonist) is appropriate: in patients not adequately controlled with inhaled corticosteroids and "as needed" inhaled short-acting β2 adrenoceptor agonists; or in patients already adequately controlled on both inhaled corticosteroids and long-acting β2 adrenoceptor agonists. The proposed extension to the indication is based upon data from the literature.
As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly.
In addition, the MAH took the opportunity to make an administrative update to the Greek, Islandic, Irish and Maltese local representatives phone numbers in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.1.
An updated RMP version 3.0 was submitted as part of the application.
Type IB variation - C.I.z other – updates of sections 4.2, 5.1 and 5.2 of the SmPC to update the information on paediatric data and section 4.4 of the SmPC to remove the warning regarding the risk of growth retardation in children and the guidance on how to address this risk as agreed during the assessment of the duplicate Budesonide/Formoterol Teva Pharma B.V. (EMEA/H/C/004882), which was approved in Jan 2020."

Action: For adoption

Request for Supplementary Information adopted on 15.10.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.4. Esbriet - pirfenidone - EMEA/H/C/002154/II/0069

Roche Registration GmbH

Rapporteur: Peter Kiely, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension of indication to include the treatment of unclassifiable interstitial lung disease (UILD) for Esbriet; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 11.0 of the RMP has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, mainly concerning clinical aspects.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.5. Jardiance - empagliflozin - EMEA/H/C/002677/II/0055

Boehringer Ingelheim International GmbH

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication to include treatment of adult patients with heart failure and reduced ejection fraction for Jardiance; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 4.9 and 5.1 of the SmPC are updated. This is based on final results from the EMPEROR HFrEF study, a phase III randomised, double-blind trial to evaluate efficacy and safety of once daily empagliflozin 10 mg compared to placebo. The Package Leaflet and Labelling are updated in accordance. Version 15.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 28.01.2021.

The Committee discussed the issues identified in this application, relating to clinical aspects and the request for 1 year of market protection for a new indication.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.6. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0097

Merck Sharp & Dohme B.V.

Rapporteur: Armando Genazzani, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include in combination with chemotherapy, first-line treatment of locally advanced unresectable or metastatic carcinoma of the oesophagus or HER-2 negative gastroesophageal junction adenocarcinoma in adults for Keytruda, based on the results from the pivotal KEYNOTE-590 (KN590) trial. Phase 3, randomized, double-blind, placebo-controlled, multisite study to evaluate the efficacy and safety of pembrolizumab in combination with chemotherapy (cisplatin and 5-FU) versus chemotherapy (cisplatin with 5-FU) as first-line treatment in participants with locally advanced unresectable metastatic adenocarcinoma or squamous cell carcinoma of the oesophagus or advanced/metastatic Siewert type 1 adenocarcinoma of the gastroesophageal junction; as a consequence sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version of the RMP (Version 30.1) has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 25.02.2021.

The Committee discussed the issues identified in this application, mainly relating to clinical aspects.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.7. Nulojix - belatacept - EMEA/H/C/002098/II/0070

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include the use of belatacept in conversion from a calcineurin inhibitor-based regimen to a belatacept-based regimen post transplantation; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 18.0 of the RMP has also been updated. Furthermore, the product information is brought in line with the latest QRD template version 10.1 and requirement on sodium excipients is added. Editorial changes have been made in the labelling."

Action: For adoption

Request for Supplementary Information adopted on 12.11.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.8. Tagrisso - osimertinib - EMEA/H/C/004124/II/0039/G

AstraZeneca AB

Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication of Tagrisso to include the adjuvant treatment after complete tumour resection in EGFR mutant non-small cell lung cancer (NSCLC) patients, based on the results from the pivotal Phase 3 randomised, placebo-controlled study ADAURA (D5164C00001); as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 14.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 25.03.2021, 10.12.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.9. Ultomiris - ravulizumab - EMEA/H/C/004954/II/0010

Alexion Europe SAS

Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of indication to include treatment of paediatric patients with paroxysmal nocturnal haemoglobinuria (PNH) for Ultomiris; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, Annex II is updated to reflect the addition of a PNH Parent guide. Version 2.1 of the RMP has also been submitted, in order to include the new indication."

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to clinical aspects.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.10. Venclyxto - venetoclax - EMEA/H/C/004106/II/0030

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Filip Josephson, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Eva Jirsová

Scope: "Extension of indication for Venclyxto (venetoclax) in combination with Hypomethylating Agents (HMAs) or Low Dose Cytarabine (LDAC) for the treatment of adult

patients with newly-diagnosed acute myeloid leukaemia (AML) who are ineligible for intensive chemotherapy. As a consequence, sections 4.2, 4.3, 4.4, 4.5, 4.7, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and RMP version 6.1 are also updated accordingly.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 28.01.2021, 15.10.2020.

The CHMP noted the report from the SAG-Oncology.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

5.1.11. WS1881
Opdivo - nivolumab - EMEA/H/C/003985/WS1881/0091
Yervoy - ipilimumab - EMEA/H/C/002213/WS1881/0085

Bristol-Myers Squibb Pharma EEIG

Lead Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include first-line treatment of adult patients with unresectable malignant pleural mesothelioma (MPM) for Opdivo in combination with Yervoy; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 20.0 for Opdivo and version 30.0 for Yervoy of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 25.03.2021, 10.12.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.12. WS1952
Edistride - dapagliflozin - EMEA/H/C/004161/WS1952/0042
Forxiga - dapagliflozin - EMEA/H/C/002322/WS1952/0060

AstraZeneca AB

Lead Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Extension of indication for Forxiga / Edistride to include treatment of children aged 10 years and adolescents with T2DM based on the results from studies MB10209/D1690C000016 and MB102-138/D1690C00017; these are paediatric studies submitted according to Article 46 of the Paediatric Regulation. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 21 of the RMP has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to clinical aspects.

The Committee adopted a request for supplementary information with a specific timetable.

5.2. Update on on-going Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

5.2.1. Brilique - ticagrelor - EMEA/H/C/001241/II/0047/G

AstraZeneca AB

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst

Scope: C.1.4 Update of the SmPC sections 4.4 and 4.8 to include information on ticagrelor and traumatic hemorrhages, based on data from the THEMIS study and on the totality of data from the clinical development program and post-marketing use.

Final Assessment Report for information

Action: For information

Opinion adopted on 25.03.2021

The CHMP noted the final assessment report.

5.3. Re-examination of Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008

No items

6. Ancillary medicinal substances in medical devices

6.1. Ancillary medicinal substances in medical devices; Opinions/ Day 180 list of outstanding issues / Day 120 list of questions

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

7. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

7.1. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. copanlisib – H0004334

Treatment of adult patients with relapsed marginal zone lymphoma

Scope: Briefing note and the Rapporteurs' recommendation on the request for accelerated assessment.

Action: For adoption

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.1.2. budesonide – H0005653

Treatment of primary Immunoglobulin A nephropathy (IgAN)

Scope: Briefing note and the Rapporteurs' recommendation on the request for accelerated assessment.

Action: For adoption

The CHMP agreed to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.1.3. maribavir - Orphan - H0005787

Shire Pharmaceuticals Ireland Limited; Treatment of adults with post-transplant cytomegalovirus (CMV) infection and/or disease who are resistant and/or refractory to one or more prior therapy including ganciclovir, valganciclovir, cidofovir or foscarnet

Scope: Briefing note and the Rapporteurs' recommendation on the request for accelerated assessment.

Action: For adoption

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.2. Priority Medicines (PRIME)

Information related to priority medicines cannot be released at present time as these contain commercially confidential information

8.2.1. List of applications received

Action: For information

The CHMP noted the information.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 5 recommendations for eligibility to PRIME: 1 was accepted and 4 were denied.

The individual outcomes are listed in the PRIME Monthly Report on the EMA website.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Veklury – remdesivir - EMEA/H/C/005622/LEG/031

Gilead Sciences Ireland UC

Rapporteur: Janet Koenig, Co-Rapporteur: Filip Josephson

Scope: Update on the procedure.

Action: For adoption

The Committee concluded that the LEG is closed, with the conclusion that the PAM is not fulfilled. The follow-up will be done in the ongoing renewal procedure.

9.1.2. Veklury - remdesivir - EMEA/H/C/005622/R/0015

Gilead Sciences Ireland UC

Rapporteur: Janet Koenig, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Eva Jirsová

Request for Supplementary Information adopted on 25.03.2021.

The CHMP amended the request for supplementary information, which was adopted in March 2021 with a specific timetable.

9.1.3. Invokana - canagliflozin - EMEA/H/C/002649/II/0055

Janssen-Cilag International NV

Rapporteur: Martina Weise

Scope: "Update to sections 4.2 and 5.1 of the Invokana SmPC to amend posology information concerning the treatment of patients with eGFR between ≥30 and <45 mL/min/1.73 m2, whether or not albuminuria is present; the update is based on further analysis of previously submitted CANVAS data (studies DIA3008 and DIA4003).
The applicant has also taken the opportunity to make minor editorial changes to section 4.5."

Action: For adoption

Request for Supplementary Information adopted on 28.01.2021.

The Committee discussed the issues identified in this application, mainly relating to clinical aspects.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

9.1.4. Iscover-EMEA/H/C/000175/WS1820/0142 Plavix-EMEA/H/C/000174/WS1820/0140

Sanofi Aventis Groupe

Rapporteur: Bruno Sepodes

Scope: "Update of section 4.2 of the SmPC in order to add 600 mg as an alternative loading dose to the existing 300 mg to be used at initiation of treatment in the indication "Secondary prevention of atherothrombotic events in adult patients suffering from acute coronary syndrome". This update is based on a bibliographic review of published studies. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.10.2020, 25.06.2020.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

9.1.5. COVID-19 Vaccine Janssen – COVID-19 vaccine (Ad26.COV2-S [recombinant]) – EMEA/H/C/005737

Janssen-Cilag International N.V.; prevention of coronavirus disease-2019 (COVID-19)

Rapporteur: Christophe Focke, Co-Rapporteur: Sol Ruiz, PRAC Rapporteur: Ulla Wändel Liminga

Scope: PRAC signal recommendation on embolic and thrombotic events

Action: For adoption

The CHMP adopted the PRAC signal recommendation on embolic and thrombotic events.

9.1.6. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0102

Merck Sharp & Dohme B.V.

Rapporteur: Armando Genazzani

Scope: "Update of sections 4.2 and 5.1 of the SmPC in order to introduce an alternative dosing regimen of 400 mg every 6 weeks (Q6W) for all approved indications based on interim results from study KEYNOTE-555; this is an interventional, PK study in patients with advanced melanoma. Additional data/analysis from studies KEYNOTE-021, -048, -189, -407 and -426 were provided."

Action: For adoption

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

9.1.7. Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/ANX/001.6

Orexigen Therapeutics Ireland Limited

Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Martin Huber

Scope: Annual progress report for Cardiovascular Outcome Trial 2

Action: For adoption

The CHMP concluded that the PAM is not considered fulfilled and adopted a list of questions with a specific timetable.

9.1.8. VITRAKVI - larotrectinib - EMEA/H/C/004919/II/0010/G

Bayer AG

Rapporteur: Filip Josephson

Scope: quality changes

Revised opinion

Action: For adoption

Opinion adopted on 28.01.2021.

Request for Supplementary Information adopted on 15.10.2020.

The CHMP adopted the revised opinion.

10. Referral procedures

10.1. Procedure for Centrally Authorised products under Article 20 of Regulation (EC) No 726/2004

No items

10.2. Requests for CHMP Opinion under Article 5(3) of Regulation (EC) No 726/2004

10.2.1. Vaxzevria – COVID-19 Vaccine (ChAdOx1-S [recombinant]) – EMEA/H/A-5(3)/1507

Astra Zeneca AB

Referral Rapporteur: Johann Lodewijk Hillege, Referral Co-Rapporteur: Sol Ruiz

Scope: Interim opinion

Rapporteurs were appointed via written procedure on 14.04.2021.

Action: For adoption

Following the conclusion of a possible link between Vaxzevira and very rare cases of unusual blood clots with low blood platelets, the EC/Commission representative requested a further analysis and stratification of data under Article 5(3) of Regulation (EC) 726/2004, as well as, if possible providing a recommendation on the administration of the second dose of Vaxzevira on the basis of the available data.

The CHMP discussed the available data and agreed to hold an extraordinary meeting on 23.04.2021.

On 23.04.2021, the Committee adopted a positive opinion by consensus concluding that the benefits of Vaxzevria outweigh its risks in adults of all age groups; however, very rare cases of blood clots with low blood platelets have occurred following vaccination.

To support national authorities making decisions on how to best use the vaccine in their territories, the CHMP has further analysed available data to put the risk of these very rare blood clots in the context of the vaccine's benefits for different age groups and different rates of infection.

The Committee also considered available data on the use of the second dose. The CHMP recommended to continue giving a second dose of Vaxzevria between 4 and 12 weeks after giving the first one in line with the product information.

The CHMP adopted the assessment report.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The EMA communication documents were circulated for information.

10.2.2. GSK4182136 (VIR-7831) for the treatment of COVID-19 - EMEA/H/A-5(3)/1508

GSK

Referral Rapporteur: Kirstine Moll Harboe, Referral Co-Rapporteur: Jayne Crowe

Scope: start of procedure, timetable and list of questions were adopted via written procedure on 15.04.2021

Rapporteurs were appointed via written procedure on 14.04.2021.

Action: For information

The CHMP noted the documents adopted via written procedure.

Notification: 14.04.2021

Start of the procedure (CHMP): 15.04.2021 (via written procedure)

CHMP list of questions: 15.04.2021 (via written procedure)

Submission of responses: 21.04.2021

Re-start of the procedure: 22.04.2021

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 04.05.2021

Comments: 07.05.2021

Updated rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 12.05.2021

CHMP list of outstanding issues / /CHMP opinion: May 2021 CHMP

10.3. Procedure under Articles 5(2) and 10 of Regulation (EC) No 726/2004

No items

10.4. Disagreement between Member States on application for medicinal product (potential serious risk to public health) –under Article 29(4) of Directive 2001/83/EC

No items

10.5. Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC

No items

10.6. Community Interests - Referral under Article 31 of Directive 2001/83/EC

No items

10.7. Re-examination Procedure under Article 32(4) of Directive 2001/83/EC

No items

10.8. Procedure under Article 107(2) of Directive 2001/83/EC

No items

10.9. Disagreement between Member States on Type II variation– Arbitration procedure initiated by MAH under Article 6(13) of Commission Regulation (EC) No 1084/2003

No items

10.10. Procedure under Article 29 of Regulation (EC) 1901/2006

No items

10.11. Referral under Article 13 Disagreement between Member States on Type II variation– Arbitration procedure initiated by Member State under Article 13 (EC) of Commission Regulation No 1234/2008

No items

11. Pharmacovigilance issue

11.1. Early Notification System

April 2021 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

The CHMP noted the information.

12. Inspections

12.1. GMP inspections

Information related to GMP inspections will not be published as it undermines the purpose of such inspections

12.2. GCP inspections

Information related to GCP inspections will not be published as it undermines the purpose of

such inspections

12.3. Pharmacovigilance inspections

Information related to Pharmacovigilance inspections will not be published as it undermines the purpose of such inspections

12.4. GLP inspections

Information related to GLP inspections will not be published as it undermines the purpose of such inspections

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

No items

13.3. Requests for CHMP Opinion under Article 57(1)J and (1)P of Regulation (EC) No 726/2004

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Resourcing of Covid-19 applications: Follow up from February and March CHMP meetings

Update to the CHMP on the progress and next steps on resourcing of Covid-19 applications following discussion at February and March CHMP meetings

Action: For discussion

The CHMP agreed to apply the new rules for procedures starting in May (initial MAAs, extensions of indications and line extensions).

https://www.ema.europa.eu/en/news/additional-measures-allow-experts-focus-covid-19-

activities

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for April 2021

Action: For adoption

The CHMP adopted the EURD list.

14.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP April 2021 meeting to CHMP for adoption:

- 12 reports on products in scientific advice and protocol assistance
- 12 reports on products in pre-authorisation procedures
- 0 reports on products in post-authorisation procedures
- 1 reports on products in plasma master file

Action: For adoption

The CHMP adopted the BWP reports.

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 20-21 April 2021.

Action: For adoption

The CHMP adopted the Table of Decisions.

14.3.3. Safety Working Party (SWP)

Chairs: Jan Willem Van der Laan/Susanne Brendler-Schwaab

SWP position on draft HMPC public statement on herbal medicinal products containing pyrrolizidine alkaloids

Action: For adoption

The CHMP adopted the SWP position.

14.3.4. Pharmacokinetics Working Party (PKWP)

Chair: Caroline Versantvoort

Use of IMPs containing nitrosamines in clinical trials; Question from PKWP to CHMP

Action: For adoption

The CHMP noted the question from the PKWP on the use of Rifampicin in Drug Interaction Studies in healthy volunteers and discussed the recommendation from the Nitrosamine Implementation Oversight Group (NIOG) that Rifampicin containing nitrosamine levels above the acceptable intake should not be used in these studies. The CHMP was in agreement with the recommendation and adopted the response to PKWP.

14.3.5. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 06-09 April 2021. Table of conclusions

Action: For information

The CHMP noted the report.

Scientific advice letters:

Information related to scientific advice letters cannot be released at present time as these contain commercially confidential information.

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

14.6. Contacts of the CHMP with external parties and interaction with the Interested Parties to the Committee

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

Action: For information

The CHMP noted the update.

15.1.2. COVID-19 mRNA vaccine - EMEA/H/C/005845

prevention of COVID-19

Scope: Rolling review timetable adopted via written procedure on 06 April 2021

Action: For information

The CHMP noted the RR timetable adopted via written procedure.

Lists of participants

List of participants including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the 19-22 April 2021 CHMP meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Harald Enzmann	Chair	Germany	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Daniela Philadelphy	Alternate	Austria	No interests declared	
Christophe Focke	Member	Belgium	No restrictions applicable to this meeting	
Karin Janssen van Doorn	Alternate	Belgium	No interests declared	
Ilko Getov	Member	Bulgaria	No interests declared	
Margareta Bego	Member	Croatia	No interests declared	
Selma Arapovic Dzakula	Alternate	Croatia	No interests declared	
Helena Panayiotopoulou	Member	Cyprus	No interests declared	
Emilia Mavrokordatou	Alternate	Cyprus	No participation in final deliberations and voting on	COVID-19 vaccines
Ondřej Slanař	Member	Czechia	No restrictions applicable to this meeting	
Tomas Radimersky	Alternate	Czechia	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Kirstine Moll Harboe	Alternate	Denmark	No interests declared	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Edward Laane	Alternate	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Johanna Lähteenvuo	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Jean-Michel Race	Alternate	France	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Martina Weise	Member	Germany	No restrictions applicable to this meeting	
Janet Koenig	Alternate	Germany	No interests declared	
Konstantinos Markopoulos	Member	Greece	No interests declared	
Eleftheria Nikolaidi	Alternate	Greece	No interests declared	
Agnes Gyurasics	Alternate	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	Iceland	No interests declared	
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	
Peter Kiely	Alternate	Ireland	No interests declared	
Armando Genazzani	Member	Italy	No interests declared	
Elita Poplavska	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting on	COVID-19 vaccines
Simona Stankeviciute	Alternate	Lithuania	No interests declared	
Martine Trauffler	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Bjorg Bolstad	Member	Norway	No restrictions applicable to this meeting	
Ingrid Wang	Alternate	Norway	No interests declared	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Bruno Sepodes	Member (Vice-Chair)	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No participation in final deliberations and voting on	COVID-19 vaccines
Simona Badoi	Member	Romania	No interests declared	
Dana Gabriela Marin	Alternate	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Dorota Distlerova	Alternate	Slovakia	No restrictions applicable to this meeting	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Maria Concepcion Prieto Yerro	Member	Spain	No interests declared	
Blanca Garcia-Ochoa	Alternate	Spain	No interests declared	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Christian Gartner	Co-opted member	Austria	No restrictions applicable to this meeting	
Carla Torre	Co-opted member	Portugal	No interests declared	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Blanka Hirschlerova	Co-opted member	Czechia	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Mark Ainsworth	Expert - via Adobe*	Denmark	No interests declared	
Jonas Bergh	Expert - via Adobe*	Sweden	No part in discussions, final deliberations and voting on	pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477 Keytruda - pembrolizumab - EMEA/H/C/003820/II/0097 Keytruda - pembrolizumab - EMEA/H/C/003820/II/0102
Jana Klimasova	Expert - via Adobe*	Slovakia	No restrictions applicable to this meeting	
Christophe Unkrig	Expert - via Adobe*	Germany	No interests declared	
George Aislaitner	Expert - via Adobe*	Germany	No interests declared	
Christine Greiner	Expert - via Adobe*	Germany	No interests declared	
Stephanie Buchholz	Expert - via Adobe*	Germany	No interests declared	
Martin Huber	Expert - via Adobe*	Germany	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Catherine Wisbech	Expert - via Adobe*	Norway	No interests declared	
Nina Hessvik	Expert - via Adobe*	Norway	No interests declared	
Miriam Bartolo	Expert - via Adobe*	Malta	No restrictions applicable to this meeting	
Agustin Portela Moreira	Expert - via Adobe*	Spain	No interests declared	
Alicia Pérez González	Expert - via Adobe*	Spain	No interests declared	
Ana Sagredo	Expert - via Adobe*	Spain	No interests declared	
Maria Chamorro Somoza Diaz-Sarmiento	Expert - via Adobe*	Spain	No interests declared	
Stefan Bonné	Expert - via Adobe*	Belgium	No interests declared	
Diederica Claeys	Expert - via Adobe*	Belgium	No interests declared	
Olga Kholmanskikh	Expert - via Adobe*	Belgium	No interests declared	
Claire Beuneu	Expert - via Adobe*	Belgium	No interests declared	
Aaron Emmanuel Sosa Mejia	Expert - via Adobe*	Denmark	No restrictions applicable to this meeting	
Louise Frederikke Swaffield Bang-Lauritsen	Expert - via Adobe*	Denmark	No interests declared	
Elisabeth Bojsen-Møller Secher	Expert - via Adobe*	Denmark	No interests declared	
Andreas James Schaeffer Senders	Expert - via Adobe*	Denmark	No interests declared	
Martijn van Gils	Expert - via Adobe*	Netherlands	No interests declared	
Hinke Johanna Van der Woude	Expert - via Adobe*	Netherlands	No interests declared	
Alida Spruijt	Expert - via Adobe*	Netherlands	No interests declared	
Ineke Havinga	Expert - via Adobe*	Netherlands	No interests declared	
Johannes Petrus Theodorus Span	Expert - via Adobe*	Netherlands	No interests declared	
Michel Kooijman	Expert - via Adobe*	Netherlands	No interests declared	
Patrick Vrijlandt	Expert - via Adobe*	Netherlands	No interests declared	
Chantal van de Schootbrugge	Expert - via Adobe*	Netherlands	No interests declared	
Laurens de Leur	Expert - via Adobe*	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Elly Vereyken	Expert - via Adobe*	Netherlands	No restrictions applicable to this meeting	
Loes den Otter	Expert - via Adobe*	Netherlands	No interests declared	
Janneke van Leeuwen	Expert - via Adobe*	Netherlands	No interests declared	
Frank Holtkamp	Expert - via Adobe*	Netherlands	No interests declared	
Edward Bojtor	Expert - via Adobe*	Netherlands	No restrictions applicable to this meeting	
Nial Fanning	Expert - via Adobe*	Ireland	No restrictions applicable to this meeting	
Brian Aylward	Expert - via Adobe*	Ireland	No interests declared	
Catherine Byrne	Expert - via Adobe*	Ireland	No interests declared	
Finbarr Leacy	Expert - via Adobe*	Ireland	No interests declared	
Shane Gormley	Expert - via Adobe*	Ireland	No interests declared	
Koenraad Norga	Expert - via Adobe*	Belgium	No restrictions applicable to this meeting	
Mikael Andersson	Expert - via Adobe*	Sweden	No interests declared	
Charlotta Bergquist	Expert - via Adobe*	Sweden	No interests declared	
Sara Galluzzo	Expert - via Adobe*	Italy	No interests declared	
Anita Simond	Expert - via Adobe*	United Kingdom	No restrictions applicable to this meeting	
Svein Rune Andersen	Expert - via Adobe*	Norway	No interests declared	
Anna Vikerfors	Expert - via Adobe*	Sweden	No interests declared	
Rosalia Ruano Camps	Expert - via Adobe*	Spain	No interests declared	
Stephan Lehr	Expert - via Adobe*	Austria	No interests declared	
Linda Trauffler	Expert - via Adobe*	Austria	No interests declared	
Anne Isabel Roth	Expert - via Adobe*	Germany	No interests declared	
Ingrid Bourges	Expert - via Adobe*	Belgium	No interests declared	
Innes Crèvecoeur	Expert - via Adobe*	Belgium	No part in discussions, final deliberations and voting on	pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Concetta Quintarelli	Expert - via Adobe*	Italy	No interests declared	
Antonella Isgrò	Expert - via Adobe*	Italy	No interests declared	
Odoardo Maria Olimpieri	Expert - via Adobe*	Italy	No interests declared	
Brigitte Keller-Stanislawski	Expert - via Adobe*	Germany	No interests declared	
Katrien Oude Rengerink	Expert - via Adobe*	Netherlands	No part in discussions, final deliberations and voting on	pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477 Keytruda - pembrolizumab - EMEA/H/C/003820/II/0097 Keytruda - pembrolizumab - EMEA/H/C/003820/II/0102
Ebru Karakoc Madsen	Expert - via Adobe*	Denmark	No part in discussions, final deliberations and voting on	eptinezumab - EMEA/H/C/005287
Adrianus Van Gompel	Expert - via Adobe*	Netherlands	No interests declared	
Jeanette McCallion	Expert - via Adobe*	Ireland	No interests declared	
Maura O'Donovan	Expert - via Adobe*	Ireland	No interests declared	
Sujata Sengupta	Expert - via Adobe*	Netherlands	No interests declared	
Jaap Fransen	Expert - via Adobe*	Netherlands	No interests declared	
Nafise Ghalandari	Expert - via Adobe*	Netherlands	No interests declared	
Ingrid Schellens	Expert - via Adobe*	Netherlands	No interests declared	
Sanna Gevers	Expert - via Adobe*	Netherlands	No interests declared	
Elina Rönnemaa	Expert - via Adobe*	Sweden	No interests declared	
Elena Wolff-Holz	Expert - via Adobe*	Germany	No interests declared	
Elisabeth Penninga	Expert - via Adobe*	Denmark	No interests declared	
Edwidge Haelterman Brenneisen	Expert - via Adobe*	Belgium	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jacqueline Wiesner	Expert - via Adobe*	Germany	No interests declared	
Heidi Foth	Expert - via Adobe*	Germany	No interests declared	
Robert Pless	Expert - via Adobe*	Health Canada	No interests declared	
Filip Kukulski	Expert - via Adobe*	Health Canada	No interests declared	
Rolando Barbaro Dominguez Morales	Expert - via Adobe*	WHO	No interests declared	
Alain Fauconnier	Expert - via Adobe*	WHO	No interests declared	
Evelyn Soo	Expert - via Adobe*	Health Canada	No interests declared	
Ian Chisholm	Expert - via Adobe*	Health Canada	No interests declared	
Meeting run with the help of EMA staff				

*Experts were only evaluated against the product(s) they have been invited to talk about

Experts from international organisations or regulatory authorities in third countries cannot participate in the adoption of any procedural decision, scientific opinion or recommendation by the Committee at any step of the procedure.

List of participants including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the extraordinary CHMP meeting held on 23 April 2021.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Harald Enzmann	Chair	Germany	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Daniela Philadelphy	Alternate	Austria	No interests declared	
Christophe Focke	Member	Belgium	No restrictions applicable to this meeting	
Karin Janssen van Doorn	Alternate	Belgium	No interests declared	
Ilko Getov	Member	Bulgaria	No interests declared	
Margareta Bego	Member	Croatia	No interests declared	
Selma Arapovic Dzakula	Alternate	Croatia	No interests declared	
Helena Panayiotopoulou	Member	Cyprus	No interests declared	
Emilia Mavrokordatou	Alternate	Cyprus	No participation in final deliberations and voting on	COVID-19 vaccines
Ondřej Slanař	Member	Czechia	No restrictions applicable to this meeting	
Tomas Radimersky	Alternate	Czechia	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Kirstine Moll Harboe	Alternate	Denmark	No interests declared	
Edward Laane	Alternate	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Johanna Lähteenvuo	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Jean-Michel Race	Alternate	France	No interests declared	
Martina Weise	Member	Germany	No restrictions applicable to this meeting	
Janet Koenig	Alternate	Germany	No interests declared	
Konstantinos Markopoulos	Member	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Eleftheria Nikolaidi	Alternate	Greece	No interests declared	
Agnes Gyurasics	Alternate	Hungary	No interests declared	
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	
Armando Genazzani	Member	Italy	No interests declared	
Elita Poplavska	Member	Latvia	No interests declared	
Martine Trauffler	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Bjorg Bolstad	Member	Norway	No restrictions applicable to this meeting	
Ingrid Wang	Alternate	Norway	No interests declared	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Bruno Sepodes	Member (Vice-Chair)	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No participation in final deliberations and voting on	COVID-19 vaccines
Simona Badoi	Member	Romania	No interests declared	
Dana Gabriela Marin	Alternate	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Maria Concepcion Prieto Yerro	Member	Spain	No interests declared	
Blanca Garcia-Ochoa	Alternate	Spain	No interests declared	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Christian Gartner	Co-opted member	Austria	No restrictions applicable to this meeting	
Carla Torre	Co-opted member	Portugal	No interests declared	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Blanka Hirschlerova	Co-opted member	Czechia	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Jana Klimasova	Expert - via Adobe*	Slovakia	No restrictions applicable to this meeting	
Alicia Pérez González	Expert - via Adobe*	Spain	No interests declared	
Ana Sagredo	Expert - via Adobe*	Spain	No interests declared	
Maria Chamorro Somoza Diaz-Sarmiento	Expert - via Adobe*	Spain	No interests declared	
Patrick Vrijlandt	Expert - via Adobe*	Netherlands	No interests declared	
Ingrid Schellens	Expert - via Adobe*	Netherlands	No interests declared	
Sara Galluzzo	Expert - via Adobe*	Italy	No interests declared	
Rolando Barbaro Dominguez Morales	Expert - via Adobe*	WHO	No interests declared	
Alain Fauconnier	Expert - via Adobe*	WHO	No interests declared	
Meeting run with the help of EMA staff				

*Experts were only evaluated against the product(s) they have been invited to talk about

Experts from international organisations or regulatory authorities in third countries cannot participate in the adoption of any procedural decision, scientific opinion or recommendation by the Committee at any step of the procedure.

Explanatory notes

The notes below give a brief explanation of the main sections and headings in the CHMP agenda and should be read in conjunction with the agenda or the minutes.

Oral explanations *(section 2)*

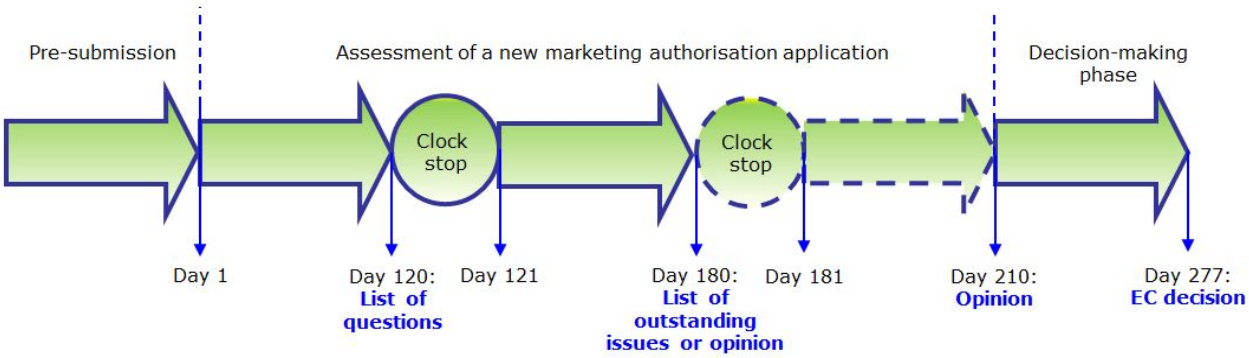
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (section 10) but can relate to any other issue for which the CHMP would like to discuss with company representatives in person.

Initial applications *(section 3)*

This section lists applications for marketing authorisations of new medicines that are to be discussed by the Committee.

Section 3.1 is for medicinal products nearing the end of the evaluation and for which the CHMP is expected to adopt an **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CHMP. The clock stop happens after day 120 and may also happen after day 180, when the CHMP has adopted a list of questions or outstanding issues to be addressed by the company. Related discussions are listed in the agenda under sections 3.2 (**Day 180 List of outstanding issues**) and 3.3 (**Day 120 list of questions**).

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 3.4, **update on ongoing new applications for centralised procedures**.

The assessment leads to an opinion from the CHMP by day 210. Following a CHMP opinion the European Commission takes usually 67 days to issue a legally binding decision (i.e. by day 277 of the procedure). CHMP discussions on products that have received a CHMP opinion and are awaiting a decision are listed under section 3.6, **products in the decision making phase**.

Extension of marketing authorisations according to Annex I of Reg. 1234/2008 *(section 4)*

Extensions of marketing authorisations are applications for the change or addition of new strengths, formulations or routes of administration to existing marketing authorisations. Extension applications

follow a 210-day evaluation process, similarly to applications for new medicines (see figure above).

Type II variations - Extension of indication procedures *(section 5)*

Type II variations are applications for a change to the marketing authorisation which requires an update of the product information and which is not covered in section 4. Type II variations include applications for a new use of the medicine (extension of indication), for which the assessment takes up to 90 days. For the applications listed in this section, the CHMP may adopt an opinion or request supplementary information from the applicant.

Ancillary medicinal substances in medical devices *(section 6)*

Although the EMA does not regulate medical devices it can be asked by the relevant authorities (the so-called Notified Bodies) that are responsible for regulating these devices to give a scientific opinion on a medicinal substance contained in a medical device.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 *(section 3.5)*

This section lists applications for new marketing authorisation for which the applicant has requested a re-examination of the opinion previously issued by the CHMP.

Re-examination procedures *(section5.3)*

This section lists applications for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP.

Withdrawal of application *(section 3.7)*

Applicants may decide to withdraw applications at any stage during the assessment and a CHMP opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

Procedure under article 83(1) of regulation (EC) 726/2004 (compassionate use) *(section 7)*

Compassionate use is a way of making available to patients with an unmet medical need a promising medicine which has not yet been authorised (licensed) for their condition. Upon request, the CHMP provides recommendations to all EU Member States on how to administer, distribute and use certain medicines for compassionate use.

Pre-submission issues *(section 8)*

In some cases the CHMP may discuss a medicine before a formal application for marketing authorisation is submitted. These cases generally refer to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation. In case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

Post-authorisation issues *(section 9)*

This section lists other issues concerning authorised medicines that are not covered elsewhere in the agenda. Issues include supply shortages, quality defects, some annual reassessments or renewals or type II variations to marketing authorisations that would require specific discussion at the plenary.

Referral procedures *(section 10)*

This section lists referrals that are ongoing or due to be started at the plenary meeting. A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. Further information on such procedures

can be found here.

Pharmacovigilance issues *(section 11)*

This section lists issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines. Feedback is provided by the PRAC. This section also refers to the early notification system, a system used to notify the European regulatory network on proposed EMA communication on safety of medicines.

Inspections Issues *(section 12)*

This section lists inspections that are undertaken for some medicinal products. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Innovation task force *(section 13)*

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes from the last ITF meeting as well as any related issue that requires discussion with the CHMP are listed in this section of the agenda. Further information on the ITF can be found here.

Scientific advice working party (SAWP) *(section 14.3.1)*

This section refers to the monthly report from the CHMP's Scientific Advice Working Party (SAWP) on scientific advice given to companies during the development of medicines. Further general information on SAWP can be found here.

Satellite groups / other committees *(section 14.2)*

This section refers to the reports from groups and committees making decisions relating to human medicines: the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), the Committee for Orphan Medicinal Products (COMP), the Committee for Herbal Medicinal Products (HMPC), Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and the Pharmamacovigilance Risk Assessment Committee (PRAC).

Invented name issues *(section 14.3)*

This section list issues related to invented names proposed by applicants for new medicines. The CHMP has established the Name Review Group (NRG) to perform reviews of the invented names. The group's main role is to consider whether the proposed names could create a public-health concern or potential safety risk. Further information can be found here.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

03 June 2021
EMA/CHMP/305130/2021

Annex to 19-22 April 2021 CHMP Minutes

Pre-submission and post-authorisations issues

A. PRE SUBMISSION ISSUES 3
A.1. ELIGIBILITY REQUESTS 3
A.2. Appointment of Rapporteur / Co-Rapporteur Full Applications 3
A.3. PRE-SUBMISSION ISSUES FOR INFORMATION 3

B. POST-AUTHORISATION PROCEDURES OUTCOMES 3
B.1. Annual re-assessment outcomes 3
B.1.1. Annual reassessment for products authorised under exceptional circumstances 3
B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES 3
B.2.1. Renewals of Marketing Authorisations requiring 2nd Renewal 3
B.2.2. Renewals of Marketing Authorisations for unlimited validity 3
B.2.3. Renewals of Conditional Marketing Authorisations 5
B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES 6
B.4. EPARs / WPARs 10
B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES 10
B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects 11
B.5.2. CHMP assessed procedures scope: Non-Clinical and Clinical aspects 14
B.5.3. CHMP-PRAC assessed procedures 23
B.5.4. PRAC assessed procedures 28
B.5.5. CHMP-CAT assessed procedures 33
B.5.6. CHMP-PRAC-CAT assessed procedures 34
B.5.7. PRAC assessed ATMP procedures 34
B.5.8. Unclassified procedures and worksharing procedures of type I variations 34
B.5.9. Information on withdrawn type II variation / WS procedure 36
B.5.10. Information on type II variation / WS procedure with revised timetable 36
B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION 37
B.6.1. Start of procedure for New Applications: timetables for information 37
B.6.2. Start of procedure for Extension application according to Annex I of Reg. 1234/2008): timetables for information 37
B.6.3. Restart of procedure - responses received to Day 120 List of Questions timetables: for information 37

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B.6.4. Annual Re-assessments: timetables for adoption 37
B.6.5. Renewals of Marketing Authorisations: timetables for adoption provided only if the validation has been completed 37
B.6.6. VARIATIONS – START OF THE PROCEDURE 39
B.6.7. Type II Variations scope of the Variations: Extension of indication 39
B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects 43
B.6.9. CHMP assessed procedures scope: Non-Clinical and Clinical aspects 46
B.6.10. CHMP-PRAC assessed procedures 51
B.6.11. PRAC assessed procedures 53
B.6.12. CHMP-CAT assessed procedures 59
B.6.13. CHMP-PRAC-CAT assessed procedures 59
B.6.14. PRAC assessed ATMP procedures 59
B.6.15. Unclassified procedures and worksharing procedures of type I variations 59
B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY 61
B.7.1. Yearly Line listing for Type I and II variations 61
B.7.2. Monthly Line listing for Type I variations 61
B.7.3. Opinion on Marketing Authorisation transfer (MMD only) 61
B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only) 61
B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only) 61
B.7.6. Notifications of Type I Variations (MMD only) 61

C. Annex C - Post-Authorisation Measures (PAMs), (Line listing of Post authorisation measures with a description of the PAM. Procedures starting in that given month with assessment timetabled) 61

D. Annex D - Post-Authorisation Measures (PAMs), (Details on PAMs including description and conclusion, for adoption by CHMP in that given month, or finalised ones with PRAC recommendation and no adoption by CHMP needed) 61

E. Annex E - EMA CERTIFICATION OF PLASMA MASTER FILES 61
E.1. PMF Certification Dossiers: 62
E.1.1. Annual Update 62
E.1.2. Variations: 62

F. ANNEX F - Decision of the Granting of a Fee Reduction/Fee Waiver 62

G. ANNEX G 62
G.1. Final Scientific Advice (Reports and Scientific Advice letters) 62
G.2. PRIME 62
G.2.1. List of procedures concluding at 19-22 April 2021 CHMP plenary: 62
G.2.2. List of procedures starting in April 2021 for May 2021 CHMP adoption of outcomes 62

H. ANNEX H - Product Shared Mailboxes – e-mail address 62

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for April 2021: **For adoption**	Adopted

A.2. Appointment of Rapporteur / Co-Rapporteur Full Applications

Final Outcome of Rapporteurship allocation for April 2021: **For adoption**	Adopted

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

Information related to pre-submission of initial applications cannot be released at the present time as these contain commercially confidential information.

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

B.1.1. Annual reassessment for products authorised under exceptional circumstances

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

B.2.1. Renewals of Marketing Authorisations requiring 2nd Renewal

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Bortezomib SUN - bortezomib - EMEA/H/C/004076/R/0015 Sun Pharmaceutical Industries Europe B.V., Generic, Generic of VELCADE, Rapporteur: Margareta Bego, PRAC Rapporteur: Amelia Cupelli Request for Supplementary Information adopted on 25.02.2021.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Erivedge - vismodegib - EMEA/H/C/002602/R/0050 Roche Registration GmbH, Rapporteur: Kristina Dunder, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Annika Folin	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can

	be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Inhixa - enoxaparin sodium - EMEA/H/C/004264/R/0076 Techdow Pharma Netherlands B.V., Duplicate, Duplicate of Thorinane (EXP), Rapporteur: Andrea Laslop, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 22.04.2021.	Request for supplementary information adopted with a specific timetable.
Kisplyx - lenvatinib - EMEA/H/C/004224/R/0043 Eisai GmbH, Rapporteur: Karin Janssen van Doorn, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: David Olsen Request for Supplementary Information adopted on 25.03.2021.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Mysildecard - sildenafil - EMEA/H/C/004186/R/0009 Mylan S.A.S, Generic, Generic of Revatio, Rapporteur: Ondřej Slanař, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 22.04.2021.	Request for supplementary information adopted with a specific timetable.
Nordimet - methotrexate - EMEA/H/C/003983/R/0018 Nordic Group B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Martin Huber Request for Supplementary Information adopted on 25.02.2021.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Sialanar - glycopyrronium - EMEA/H/C/003883/R/0018 Proveca Pharma Limited, Rapporteur: Kirstine Moll Harboe, Co-Rapporteur: Tomas Radimersky, PRAC Rapporteur: Zane Neikena Request for Supplementary Information adopted on 25.03.2021.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members

	were in agreement with the CHMP Opinion.

B.2.3. Renewals of Conditional Marketing Authorisations

Blenrep - belantamab mafodotin - EMEA/H/C/004935/R/0003, Orphan GlaxoSmithKline (Ireland) Limited, Rapporteur: Johanna Lähteenvuo, PRAC Rapporteur: Annika Folin	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Dovprela - pretomanid - EMEA/H/C/005167/R/0005, Orphan Mylan IRE Healthcare Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Liana Gross-Martirosyan	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Hepcludex - bulevirtide - EMEA/H/C/004854/R/0003, Orphan MYR GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Adam Przybylkowski Request for Supplementary Information adopted on 22.04.2021.	Request for supplementary information adopted with a specific timetable.
Idefirix - imlifidase - EMEA/H/C/004849/R/0003, Orphan Hansa Biopharma AB, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 22.04.2021.	Request for supplementary information adopted with a specific timetable.
Rozlytrek - entrectinib - EMEA/H/C/004936/R/0002 Roche Registration GmbH, Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 25.03.2021.	Positive Opinion adopted by consensus together with the CHMP assessment report. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains

	conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Translarna - ataluren - EMEA/H/C/002720/R/0061, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan	Positive Opinion adopted by consensus together with the CHMP assessment report. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection PRAC recommendations on signals adopted at the PRAC meeting held on 06-09 April 2021 PRAC:	
Signal of embolic and thrombotic events Vaxzevria - COVID-19 Vaccine (ChAdOx1-S [recombinant]) Rapporteur: Sol Ruiz, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné PRAC recommendation on a variation, DHPC; adopted via written procedure on 08.04.2021 **Action:** For information	The CHMP noted the adoption via written procedure.
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its April 2021 meeting:	
EMEA/H/C/PSUSA/00002653/202009 (rivaroxaban) CAPS: **Xarelto** (EMEA/H/C/000944) (rivaroxaban), Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "15/09/2019 To: 15/09/2020"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.9 of the SmPC to add recommendations on bleeding risk and observation in case of overdose.

	The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00009142/202008 (emtricitabine / rilpivirine / tenofovir disoproxil) CAPS: **Eviplera** (EMEA/H/C/002312) (emtricitabine / rilpivirine / tenofovir disoproxil), Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, "11/08/2017 To: 10/08/2020"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC to amend the information on bone effects. The package leaflet is updated accordingly. The list of local representatives in the PL was also updated. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010055/202009 (alemtuzumab) CAPS: **Lemtrada** (EMEA/H/C/003718) (alemtuzumab), Sanofi Belgium, Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Anette Kirstine Stark, "12/09/2019 To: 12/09/2020"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC to add a warning on thrombotic thrombocytopenic purpura and 4.8 to add the adverse reaction thrombotic thrombocytopenic purpura with a frequency rare. Also, an update of sections 4.4 and 4.8 of the SmPC to amend the adverse reaction pneumonitis. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010095/202008 (enzalutamide) CAPS: **Xtandi** (EMEA/H/C/002639) (enzalutamide), Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "30/08/2017 To: 30/08/2020"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to add the adverse reaction dysgeusia with a frequency of common. The Package leaflet is updated accordingly.

	The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP
EMEA/H/C/PSUSA/00010311/202009 (dulaglutide) CAPS: **Trulicity** (EMEA/H/C/002825) (dulaglutide), Eli Lilly Nederland B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Ilaria Baldelli, "17/09/2019 To: 17/09/2020"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to reflect the fact that cases of acute pancreatitis and pancreatitis have been reported in the post-marketing setting. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010366/202009 (naltrexone / bupropion) CAPS: **Mysimba** (EMEA/H/C/003687) (naltrexone hydrochloride / bupropion hydrochloride), Orexigen Therapeutics Ireland Limited, Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Martin Huber, "09/09/2019 To: 09/09/2020"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4, 4.5, 4.8 and 4.9 of the SmPC to add serotonin syndrome as a warning, interaction, adverse reaction of naltrexone/bupropion with an unknown frequency and symptom of overdose. Update of section 4.4 and 4.8 of the SmPC to include a warning on and reference to hypertensive crisis. Furthermore, the wording in section 4.8 of the SmPC is amended in order to include post-marketing data as a source of adverse reactions in Table 1 (Adverse reactions reported in subjects who received naltrexone/bupropion as a fixed-dose combination). The package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010373/202009 (raltegravir) CAPS: **Isentress** (EMEA/H/C/000860) (raltegravir), Merck Sharp & Dohme B.V., Rapporteur:	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the

Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, "26/09/2019 To: 26/09/2020"	terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.5 of the SmPC to add the potential interactions with iron salts. The package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010403/202009 (pembrolizumab) CAPS: **Keytruda** (EMEA/H/C/003820) (pembrolizumab), Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst, "04/09/2019 To: 03/09/2020"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of sections 4.4 and 4.8 of the SmPC to add the adverse reactions cholangitis sclerosing with a frequency rare, and gastritis with a frequency uncommon in monotherapy and common in combination with chemotherapy or axitinib. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010851/202009 (isatuximab) CAPS: **SARCLISA** (EMEA/H/C/004977) (isatuximab), sanofi-aventis groupe, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Eva A. Segovia, "01/03/2020 To: 01/09/2020"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended together with the detailed explanation of the scientific grounds for the differences with the PRAC recommendation, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 to amend the warning and 4.8 of the SmPC to add anaphylactic reaction with a frequency uncommon. The Package leaflet is updated accordingly. In addition, update of the package leaflet to include atrial fibrillation as a common adverse drug reaction (ADR) in order to align with the information already included in the SmPC. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

B.4. EPARs / WPARs

Copiktra - duvelisib - EMEA/H/C/005381 Verastem Europe GmbH, Treatment of adult patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL) and relapsed or refractory follicular lymphoma (FL), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737 Janssen-Cilag International NV, prevention of coronavirus disease-2019 (COVID-19), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Drovelis - drospirenone / estetrol - EMEA/H/C/005336 Gedeon Richter Plc., oral contraceptive, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Efmody - hydrocortisone - EMEA/H/C/005105, Orphan Diurnal Europe BV, replacement therapy for congenital adrenal hyperplasia (CAH) in adolescents aged 12 years and over and adults., Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Lydisilka - drospirenone / estetrol - EMEA/H/C/005382 Estetra SRL, oral contraception, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
PONVORY - ponesimod - EMEA/H/C/005163 Janssen-Cilag International N.V., treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

Scopes related to Chemistry, Manufacturing, and Controls cannot be released at the present time as these contain commercially confidential information.

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0020 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop Opinion adopted on 22.04.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0017/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 30.03.2021.	Positive Opinion adopted by consensus on 30.03.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0020/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 31.03.2021.	Positive Opinion adopted by consensus on 31.03.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0022/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 21.04.2021. Request for Supplementary Information adopted on 14.04.2021.	Positive Opinion adopted by consensus on 21.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. Request for supplementary information adopted with a specific timetable.
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0026 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 21.04.2021.	Positive Opinion adopted by consensus on 21.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COVID-19 Vaccine Moderna - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0004/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 09.04.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COVID-19 Vaccine Moderna - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0011/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 22.04.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cufence - trientine dihydrochloride - EMEA/H/C/004111/II/0007/G	Request for supplementary information adopted with a specific timetable.

Univar Solutions BV, Rapporteur: Daniela Philadelphy Request for Supplementary Information adopted on 09.04.2021.	
Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0058/G Merck Sharp & Dohme B.V., Rapporteur: Paula Boudewina van Hennik Opinion adopted on 15.04.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Empliciti - elotuzumab - EMEA/H/C/003967/II/0026 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 15.04.2021.	Request for supplementary information adopted with a specific timetable.
GIVLAARI - givosiran - EMEA/H/C/004775/II/0004/G, Orphan Alnylam Netherlands B.V., Rapporteur: Paula Boudewina van Hennik Opinion adopted on 09.04.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kalydeco - ivacaftor - EMEA/H/C/002494/II/0093, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro Opinion adopted on 15.04.2021. Request for Supplementary Information adopted on 11.03.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0050/G, Orphan Amgen Europe B.V., Rapporteur: Blanca Garcia-Ochoa Opinion adopted on 09.04.2021. Request for Supplementary Information adopted on 03.12.2020.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
MenQuadfi - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/005084/II/0001/G Sanofi Pasteur, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 09.04.2021.	Request for supplementary information adopted with a specific timetable.
Mepsevii - vestronidase alfa - EMEA/H/C/004438/II/0019, Orphan Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 09.04.2021. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 14.01.2021.	
Omnitrope - somatropin - EMEA/H/C/000607/II/0070 Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 15.04.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Palynziq - pegvaliase - EMEA/H/C/004744/II/0017, Orphan BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 15.04.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0170/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 09.04.2021. Request for Supplementary Information adopted on 04.02.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Repatha - evolocumab - EMEA/H/C/003766/II/0051 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege Opinion adopted on 22.04.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Revestive - teduglutide - EMEA/H/C/002345/II/0052/G, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Kirstine Moll Harboe Opinion adopted on 22.04.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Rybelsus - semaglutide - EMEA/H/C/004953/II/0012 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 22.04.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0057/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac Opinion adopted on 22.04.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0075 MCM Vaccine B.V., Rapporteur: Christophe Focke Opinion adopted on 15.04.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Veklury - remdesivir - EMEA/H/C/005622/II/0013/G Gilead Sciences Ireland UC, Rapporteur: Janet Koenig Opinion adopted on 22.04.2021. Request for Supplementary Information adopted on 25.02.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Voncento - human coagulation factor VIII / human von Willebrand factor - EMEA/H/C/002493/II/0047/G CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 15.04.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0025/G Pfizer Ireland Pharmaceuticals, Rapporteur: Bjorg Bolstad Opinion adopted on 15.04.2021. Request for Supplementary Information adopted on 04.02.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.2. CHMP assessed procedures scope: Non-Clinical and Clinical aspects

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0085, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, "Update of the SmPC section 5.1 following the 5-year long-term follow up for the C25007 study in HL. Editorial updates have been also implemented in the PI. In addition, the MAH took the opportunity to update the list of local representatives for The Netherlands and United Kingdom (Northern Ireland) in the package leaflet." Opinion adopted on 22.04.2021. Request for Supplementary Information adopted on 25.03.2021, 28.01.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0086, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, "Update of the SmPC section 5.1 following the submission of the CSR addendum which includes long-term follow up or final OS results for the AETHERA study "A phase 3, randomised, double-blind, placebo-controlled, multicentre, clinical trial in patients with Hodgkin Lymphoma (HL) at risk of relapse or	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

progression following ASCT"" Opinion adopted on 22.04.2021. Request for Supplementary Information adopted on 25.03.2021.	
Bridion - sugammadex - EMEA/H/C/000885/II/0039 Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, "Update of sections 4.8 and 5.1 of the SmPC in order to update information on safety profile in American Society of Anesthesiologists (ASA) Class 3 or 4 patients (patients with severe systemic disease or patients with severe systemic disease that is a constant threat to life) based on final results from study 8616-P145, an interventional safety study of sugammadex for the reversal of neuromuscular blockage induced by rocuronium or vecuronium in adult ASA 3-4 participants." Request for Supplementary Information adopted on 09.04.2021.	Request for supplementary information adopted with a specific timetable.
Cholib - fenofibrate / simvastatin - EMEA/H/C/002559/II/0029/G Mylan IRE Healthcare Limited, Rapporteur: Alar Irs, "Update of section 4.4 of the SmPC in order to amend the existing warning on immune-mediated necrotizing myopathy (IMNM) and section 4.5 of the SmPC to add drug-drug interaction information with cobicistat, following the update of the company's core data sheet (CCDS) due to new data; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the UK (Northern Ireland) local representative in the Package Leaflet." Request for Supplementary Information adopted on 09.04.2021.	Request for supplementary information adopted with a specific timetable.
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0019 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Menno van der Elst, "Type II variation C.I.11.b consisting of an update of the RMP for Comirnaty to revise the post-authorisation effectiveness epidemiology study C4591014 currently included in the RMP (Cat 3) as milestone and describing 3 replacement studies to pursue the same objective. Version 1.1 of the RMP has also been	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

submitted." Opinion adopted on 15.04.2021.	
Cresemba - isavuconazole - EMEA/H/C/002734/II/0030, Orphan Basilea Pharmaceutica Deutschland GmbH, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.3 of the SmPC to update the description of non-clinical information following REC 002.2, based on final results from study B-7855, a 2-year carcinogenicity studies in mice. In this context, the safety margins described in section 5.3 based on PK data provided with the initial Cresemba MAA have been recalculated, corrected and expressed based on exposure (AUC; including free fraction) rather than based on body surface area (only bound fraction). Details of local representatives were updated in the Package Leaflet. The MAH also took the opportunity to carry out formatting improvements throughout the PI." Opinion adopted on 22.04.2021. Request for Supplementary Information adopted on 14.01.2021, 17.09.2020.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Darzalex - daratumumab - EMEA/H/C/004077/II/0047, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "C.I.4 Update of section 4.4 of the SmPC in order to include a fatal outcome for IRRs following a systematic cross-programmatic review of fatal cases of Infusion Related Reaction (IRR) with use of daratumumab. In addition, the MAH has taken the opportunity to correct in section 4.8 the reported incidence rate of Grade 3 or 4 treatment-emergent infections from study MMY3003 for DRd from 27% to 28%." Request for Supplementary Information adopted on 09.04.2021.	Request for supplementary information adopted with a specific timetable.
Deltyba - delamanid - EMEA/H/C/002552/II/0045, Orphan Otsuka Novel Products GmbH, Rapporteur: Christophe Focke, "Submission of the revised final study report from the Hollow Fiber System - Tuberculosis (HFS-TB) study listed as a Specific Obligation in the Annex II of the Product Information. This is a PK/PD study carried out using the HFS-TB model and designed to obtain the pharmacodynamic target (PDT) of delamanid in the HFS-TB, using	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Mycobacterium tuberculosis (Mtb) both under log-phase growth conditions and under low pH conditions (pH 5.8). The Annex II is updated accordingly. This submission addresses the post-authorisation measure SOB 009." Opinion adopted on 09.04.2021. Request for Supplementary Information adopted on 28.01.2021, 17.09.2020.	
Dovprela - pretomanid - EMEA/H/C/005167/II/0004/G, Orphan Mylan IRE Healthcare Limited, Rapporteur: Filip Josephson, "Grouped application including three type II variations under category C.I.4. Update of sections 4.5 and 5.3 of the SmPC based on data from three non-clinical studies: - Assessment of pretomanid as an inhibitor of human OCT2-, OATP1B3-, BCRP-, and P-gp mediated transport; - In vitro evaluation of induction/inhibition of CYP 2C8, 2C9, and 2C19 in human hepatocytes; - A 24-Month Oral (Gavage) Carcinogenicity Study in Rats." Request for Supplementary Information adopted on 09.04.2021.	Request for supplementary information adopted with a specific timetable.
Eliquis - apixaban - EMEA/H/C/002148/II/0080 Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to update the existing warning regarding patients with active cancer in line with the final results of the study CARAVAGGIO (NCT03045406), which is a randomized open-label non-inferiority clinical trial assessing apixaban for the treatment of acute proximal DVT and/or PE in ambulatory patients with active cancer or history of cancer. In addition, the MAH took the opportunity to make a correction to section 5.1 of the SmPC and to remove the list of local representatives from the package leaflet." Opinion adopted on 15.04.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Esbriet - pirfenidone - EMEA/H/C/002154/II/0070 Roche Registration GmbH, Rapporteur: Peter Kiely, "Update of section 4.8 of the SmPC to revise the MeDRA frequency categories for some adverse drug reactions (ADR) and to combine the ADR 'anorexia' with the preferred term 'decreased appetite' based on a safety update	Request for supplementary information adopted with a specific timetable.

report previously submitted in variation EMEA/H/C/2154/II/0021. The package leaflet is updated accordingly." Request for Supplementary Information adopted on 09.04.2021.	
Invokana - canagliflozin - EMEA/H/C/002649/II/0055 Janssen-Cilag International NV, Rapporteur: Martina Weise, "Update to sections 4.2 and 5.1 of the INVOKANA SmPC to amend posology information concerning the treatment of patients with eGFR between ≥30 and <45 mL/min/1.73 m2, whether or not albuminuria is present; the update is based on further analysis of previously submitted CANVAS data (studies DIA3008 and DIA4003). The Applicant has also taken the opportunity to make minor editorial changes to section 4.5." Request for Supplementary Information adopted on 22.04.2021, 28.01.2021.	Request for supplementary information adopted with a specific timetable. See 9.1
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0100 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of section 5.1 of the SmPC in order to update efficacy data based on interim results from study KEYNOTE-054 listed as a PAES in the Annex II; this is a randomized, double-blind, placebo-controlled phase 3 study evaluating pembrolizumab in the adjuvant therapy of patients with resected high-risk melanoma." Opinion adopted on 15.04.2021. Request for Supplementary Information adopted on 11.03.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0102 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of sections 4.2 and 5.1 of the SmPC in order to introduce an alternative dosing regimen of 400 mg every 6 weeks (Q6W) for all approved indications based on interim results from study KEYNOTE-555; this is an interventional, PK study in patients with advanced melanoma. Additional data/analysis from studies KEYNOTE-021, -048, -189, -407 and -426 were provided." Opinion adopted on 22.04.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. See 9.1
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0040	Request for supplementary information adopted with a specific timetable.

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Update of sections 4.8 and 5.1 of the SmPC to include information related to the safety and efficacy of Maviret for people who inject drugs (PWID) and those who are on medication-assisted treatment (MAT) for opioid use disorder based on data from Phase 2 and 3 clinical trials. In addition, the MAH took the opportunity to include an editorial change and corrected the number of subjects stated in Footnote B, Table 8 of the SmPC section 5.1." Request for Supplementary Information adopted on 09.04.2021.	
Nilemdo - bempedoic acid - EMEA/H/C/004958/II/0007 Daiichi Sankyo Europe GmbH, Rapporteur: Johann Lodewijk Hillege, "C.I.13: Submission of the final report from clinical study 1002-050 listed as a category 3 study in the RMP (MEA). This is a multicenter open-label extension (OLE) study to assess the long-term safety and efficacy of bempedoic acid 180 mg. Study 1002-050 was a roll-over extension study of a long-term (52 weeks), randomized, double-blind, controlled study (Study 1002-040, referred to as the parent study) of bempedoic acid 180 mg once daily versus placebo with a 2:1 randomization." Opinion adopted on 15.04.2021. Request for Supplementary Information adopted on 14.01.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nustendi - bempedoic acid / ezetimibe - EMEA/H/C/004959/II/0007 Daiichi Sankyo Europe GmbH, Rapporteur: Johann Lodewijk Hillege, "C.I.13: Submission of the final report from clinical study 1002-050 listed as a category 3 study in the RMP (MEA). This is a multicenter open-label extension (OLE) study to assess the long-term safety and efficacy of bempedoic acid 180 mg. Study 1002-050 was a roll-over extension study of a long-term (52 weeks), randomized, double-blind, controlled study (Study 1002-040, referred to as the parent study) of bempedoic acid 180 mg once daily versus placebo with a 2:1 randomization." Opinion adopted on 15.04.2021. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 14.01.2021.	
Opsumit - macitentan - EMEA/H/C/002697/II/0039, Orphan Janssen-Cilag International N.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of sections 4.4, 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information of macitentan with moderate dual inhibitors of CYP3A4 and CYP2C9 based on results from a non-clinical study and a physiologically based pharmacokinetic study in healthy subjects and CYP2C9 poor metabolizers; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to make editorial changes in the labelling." Opinion adopted on 22.04.2021. Request for Supplementary Information adopted on 28.01.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Taltz - ixekizumab - EMEA/H/C/003943/II/0040 Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC with long-term efficacy and safety data in axial spondyloarthritis from study RHBY - A multicenter, long-term extension study of 104 weeks, including a double-blind, placebo-controlled 40-week randomized withdrawal–retreatment period, to evaluate the maintenance of treatment effect of ixekizumab in patients with axial spondyloarthritis." Request for Supplementary Information adopted on 22.04.2021, 21.01.2021.	Request for supplementary information adopted with a specific timetable.
Talzenna - talazoparib - EMEA/H/C/004674/II/0009 Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of sections 4.2 and 5.2 based on the results from PK study MDV3800-02 (C3441002), a phase 1 open-label pharmacokinetics and safety study of talazoparib (MDV3800) in patients with advanced solid tumours and normal or varying degrees of hepatic impairment. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet." Opinion adopted on 22.04.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vyndaqel - tafamidis - EMEA/H/C/002294/II/0067, Orphan	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP

Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, "Update of section 4.5 of the SmPC in order to add drug-drug interaction information with Rosuvastatin, a breast cancer resistant protein (BCRP), based on final results from study B3461075. This is a Phase 1 interventional clinical drug-drug interaction study to estimate the effect of a multiple oral administration of Tafamidis on Rosuvastatin in pharmacokinetics (PK) in healthy participants." Opinion adopted on 15.04.2021. Request for Supplementary Information adopted on 11.03.2021.	Members were in agreement with the CHMP recommendation.
Wakix - pitolisant - EMEA/H/C/002616/II/0023/G, Orphan Bioprojet Pharma, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Kirsti Villikka, "Update of the product information based on new clinical data from the open-label, long-term treatment of EDS (with or without cataplexy) in narcolepsy P09-10 HARMONY III study, and the randomised, double-blind, placebo-controlled, drug abuse potential study (P16-02). The proposed update also includes results of a post-approval network meta-analysis which compares efficacy and safety of multiple treatments, multi-arm studies, and multi-criteria treatment decisions." Request for Supplementary Information adopted on 09.04.2021, 11.03.2021, 14.01.2021, 03.09.2020.	Request for supplementary information adopted with a specific timetable.
Xarelto - rivaroxaban - EMEA/H/C/000944/II/0081 Bayer AG, Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC following the final results from the VOYAGER PAD study, a multicentre, randomised, double-blind, placebo-controlled phase 3 trial investigating the efficacy and safety of rivaroxaban to reduce the risk of major thrombotic vascular events in patients with symptomatic peripheral artery disease undergoing lower extremity revascularization procedures. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 22.04.2021, 12.11.2020.	Request for supplementary information adopted with a specific timetable.
Zejula - niraparib - EMEA/H/C/004249/II/0024, Orphan	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP

GlaxoSmithKline (Ireland) Limited, Rapporteur: Bjorg Bolstad, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to include information and dosing recommendation for patients with moderate hepatic impairment and a warning on the risk of increased exposure of niraparib in patients with severe hepatic impairment based on final results from hepatic study 3000-01-003 (HEPATIC). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to introduce editorial changes in SmPC section 4.4." Opinion adopted on 22.04.2021. Request for Supplementary Information adopted on 25.02.2021.	Members were in agreement with the CHMP recommendation.
Zostavax - varicella vaccine (live) - EMEA/H/C/000674/II/0132 MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Outi Mäki-Ikola, "C.I.13: Submission of the final study report from the post-licensure observational study of the long-term effectiveness of Zostavax (Protocol 024) listed as category 3 study in the RMP. With this application, the post authorisation measure REC 23 is fulfilled." Request for Supplementary Information adopted on 09.04.2021.	Request for supplementary information adopted with a specific timetable.
WS1877 **Invega-EMEA/H/C/000746/WS1877/0068** **Paliperidone Janssen-Cilag International-EMEA/H/C/005486/WS1877/0001** **Trevicta-EMEA/H/C/004066/WS1877/0026** **Xeplion-EMEA/H/C/002105/WS1877/0051** Janssen-Cilag International NV, Lead Rapporteur: Kristina Dunder, "Update of section 4.8 (Undesirable effects) of the Summary of Product Characteristics (SmPC) for INVEGA, XEPLION, TREVICTA and Paliperidone Janssen-Cilag International to add a new adverse drug reaction (ADR) " Stevens-Johnson syndrome/toxic epidermal necrolysis" with a "not known" frequency. Section 4 of the Package Leaflet (PL) for each medicinal product is also amended accordingly." Opinion adopted on 09.04.2021. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 03.12.2020.	
WS2027 **OFEV-EMEA/H/C/003821/WS2027/0042** **Vargatef-EMEA/H/C/002569/WS2027/0039** Boehringer Ingelheim International GmbH, Lead Rapporteur: Peter Kiely, "Update of sections 4.2 and 6.6. of the SmPC in order to include an improved method of administration and handling of the capsules, respectively. This update is based on post-marketing experience. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to correct the name of the local representative in Portugal." Opinion adopted on 09.04.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2035 **Prezista-EMEA/H/C/000707/WS2035/0110** **Rezolsta-EMEA/H/C/002819/WS2035/0041** **Symtuza-EMEA/H/C/004391/WS2035/0032** Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, "To update section 4.5 of the SmPC to provide guidance on drug-drug interaction between cutaneously-administered corticosteroids and boosted darunavir, darunavir/cobicistat and darunavir/cobicistat/emtricitabine/tenofovir alafenamide, based on recent scientific literature publication. In addition, the MAH took the opportunity to include minor editorial updates in the Product Information consisting of formatting, spelling and typo corrections." Request for Supplementary Information adopted on 09.04.2021.	Request for supplementary information adopted with a specific timetable.

B.5.3. CHMP-PRAC assessed procedures

Accofil - filgrastim - EMEA/H/C/003956/II/0046/G Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "- Type II B.II.e.5.c- To introduce a new presentation, Accofil 12 MU/0.2 mL Solution for Injection or infusion in Pre-filled Syringe, to	Request for supplementary information adopted with a specific timetable.

cater to low-weight patients as the clinical administration of Filgrastim is based on body weight. The same concentration in mcg/ mL as for the already approved presentation of 300 mcg/ 0.5 mL (30 MU/0.5 ml) is obtained, i.e. 600 mcg/ mL. RMP and PI are updated to include this new strength. - Type II B.II.e.5.c- To introduce a new presentation, Accofil 70 MU/0.73 mL Solution for Injection or infusion in Pre-filled Syringe, based on the dosing regimen to avoid multiple administrations. The same concentration in mcg/ mL as for the already approved presentation of 480 mcg/ 0.5 mL (48 MU/0.5 ml) is obtained, i.e. 960 mcg/ mL. RMP and PI are updated to include this new strength." Request for Supplementary Information adopted on 09.04.2021.	
ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0017 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.8 and 5.1 of the SmPC resulting from further analyses of the continuation study 261302 and the pharmacokinetics-guided dosing study 261303. The Package Leaflet has been updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the Excipients guideline (sodium statement in 4.4) and the FVIII guideline (traceability statement in 4.4) and QRD template (labelling). The requested variation proposed amendments to the Summary of Product Characteristics, Labelling and Package Leaflet." Opinion adopted on 09.04.2021. Request for Supplementary Information adopted on 14.01.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Aimovig - erenumab - EMEA/H/C/004447/II/0013/G Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka, "Update of section 4.8 of the SmPC in line with revised clinical safety data. Submission of the study report from 5-year open-label study 20120178 with consequential changes to section 4.8 and section 5.1 of the SmPC as well as an update of the EU RMP Type IA variation to the include ATC code for	Request for supplementary information adopted with a specific timetable.

erenumab. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 09.04.2021, 11.02.2021.	
Isentress - raltegravir - EMEA/H/C/000860/II/0093 Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, "Update of section 4.6 of the SmPC in order to update safety information following pregnancy outcome data for raltegravir 400 mg film-coated tablet from prospective reports of pregnancy data with known outcome and time of raltegravir exposure. The updated RMP version 15.1 has also been submitted. In addition, the MAH took the opportunity to correct an inconsistency in the text describing the possibility to divide the scored 100 mg chewable tablet by harmonising the text of the footer of Tables 1 and 2 of the chewable tablets' SmPC. This was already identified in the procedure EMEA/H/C/000860/IB/0087 and is in line with the assessment done in the extension application for the chewable tablets EMEA/H/C/000860/X/0024/G. Finally, the contact details of Germany have been updated in the List of local Representatives and the PI is being brought in line with the latest QRD template (version 10.1)" Request for Supplementary Information adopted on 09.04.2021, 14.01.2021.	Request for supplementary information adopted with a specific timetable.
Jyseleca - filgotinib - EMEA/H/C/005113/II/0003 Gilead Sciences Ireland UC, Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update to sections 4.5 and 5.2 of the SmPC to update the wording on the inhibition of P-gp and BCRP by the primary metabolite of filgotinib (GS-829845) based upon results from an in vitro study (AD-417-2028) which assessed in vitro inhibition of human P-gp and BCRP by GS-829845. The Package Leaflet has been updated accordingly. The MAH took this opportunity to update the details of the local representatives in Germany and United Kingdom (Northern Ireland). The RMP has been updated accordingly (version 2.0)." Opinion adopted on 22.04.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lojuxta - lomitapide -	Request for supplementary information adopted

EMEA/H/C/002578/II/0046 Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "To propose an alternative study (LILITH) to the currently agreed protocol for the CAPTURE study. The new study proposes an evaluation of the effect of lomitapide treatment on major adverse cardiovascular events (MACE) in patients with homozygous familial hypercholesterolemia. Consequential submission of an updated RMP (version 6.4) and Annex IID of the Product Information. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2" Request for Supplementary Information adopted on 09.04.2021.	with a specific timetable.
Perjeta - pertuzumab - EMEA/H/C/002547/II/0054 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, "Submission of the final report from study MO28047 (PERUSE) listed as an obligation in the Annex II of the Product Information. This is a multicenter, open-label, single-arm study of pertuzumab in combination with trastuzumab and a taxane in first-line treatment of patients with HER2- positive advanced (metastatic or locally recurrent) breast cancer. The RMP (version 13.1) is updated accordingly." Opinion adopted on 09.04.2021. Request for Supplementary Information adopted on 14.01.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Piqray - alpelisib - EMEA/H/C/004804/II/0005/G Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, "C.1.4 Update of sections 4.4 and 4.8 of the SmPC in order to add hyperglycaemic hyperosmolar non-ketotic syndrome to the list of adverse drug reactions (ADRs) with frequency "unknown" and to update the warning on hyperglycaemia and ketoacidosis based on a review of the safety database. The Package leaflet and Annex II are updated accordingly. The RMP version 4.0 is approved. C.1.4 Update of sections 4.2 and 4.8 of the SmPC to modify the management of hyperglycaemia, rash and diarrhoea and add information about osteonecrosis of the jaw	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

based on the pivotal trial SOLAR-1. The MAH also took the opportunity to make minor editorial changes to the SmPC." Opinion adopted on 22.04.2021.	
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0002 AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.8, 5.1, 6.3 and 6.6 of the SmPC in order to update the safety profile and to add the adverse drug reactions: abdominal pain and urticaria with frequency uncommon; and pain in extremity and influenza-line illness with frequency common in section 4.8; based on the primary analysis (7th December data cut-off (post data-base lock) from the pooled pivotal studies (COV001, COV002, COV003 and COV005) that supported the conditional marketing authorisation and are listed as a specific obligation in the Annex II. The update on section 5.1 is editorial. The update in sections 6.3 and 6.6 relates to a rewording of the information of the shelf-life for opened vials for clarity purposes. The Package Leaflet and Labelling are updated accordingly. The MAH is taking the opportunity to update the product information in relation to the "genetically modified organisms" information. The RMP version 2.1 has also been submitted." Request for Supplementary Information adopted on 22.04.2021.	Request for supplementary information adopted with a specific timetable.
Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0030 Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Ilaria Baldelli, "Submission of the final report from study GS-US-320-4018, listed as a category 3 study in the RMP. This is a phase 3, randomized, double blind study to evaluate the efficacy and safety of switching from tenofovir disoproxil fumarate 300 mg once daily to tenofovir alafenamide 25 mg once daily in subjects with chronic hepatitis B who are virologically suppressed. The RMP (v 6.1) has also been submitted." Request for Supplementary Information adopted on 09.04.2021.	Request for supplementary information adopted with a specific timetable.
WS1820 Iscover-EMEA/H/C/000175/WS1820/	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP

0142 **Plavix-EMEA/H/C/000174/WS1820/0140** sanofi-aventis groupe, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of section 4.2 of the SmPC in order to add 600 mg as an alternative loading dose to the existing 300 mg to be used at initiation of treatment in the indication "Secondary prevention of atherothrombotic events in adult patients suffering from acute coronary syndrome". This update is based on a bibliographic review of published studies. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted." Request for Supplementary Information adopted on 15.10.2020, 25.06.2020.	Members were in agreement with the CHMP recommendation. See 9.1

B.5.4. PRAC assessed procedures

PRAC Led **Cetrotide - cetrorelix - EMEA/H/C/000233/II/0075** Merck Europe B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of an updated RMP (version 5.2), in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' including consequential removal of a number of important identified risks and important potential risk of congenital anomalies, as well as removal of missing information on infertile premenopausal women; information in the RMP has been revised based on the most recent data and the post-marketing exposure was updated. The requested variation proposed amendments to the Risk Management Plan (RMP)." Opinion adopted on 09.04.2021. Request for Supplementary Information adopted on 14.01.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0016/G** BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk	Positive Opinion adopted by consensus on 13.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Hillege, "Group of two type II variations C.I.3.b consisting of: • One update of the section 4.8 SmPC to add 2 new adverse drug reactions (ADRs) ("diarrhea", "vomiting") with frequencies and update the ADR "pain in extremity" in order to fulfil MEA 002.2 • One update of the section 4.8 SmPC to update the ADR "hypersensitivity reactions" in more detail (e.g. "rash, pruritus, urticaria, angioedema") with the relevant frequency categories in order to fulfil LEG 022.1 The section 4 of the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to perform an editorial change in section 6.6, as well as correction of some typos." Opinion adopted on 13.04.2021. Request for Supplementary Information adopted on 26.03.2021.	
PRAC Led **Constella - linaclotide - EMEA/H/C/002490/II/0053** Allergan Pharmaceuticals International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on intestinal perforation and to add gastrointestinal perforation to the list of adverse drug reactions (ADRs) with frequency rare as requested by the PRAC in procedure EMEA/H/C/002490/LEG/015, the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Opinion adopted on 09.04.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Gardasil - human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - EMEA/H/C/000703/II/0091** MSD Vaccins, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study 070 listed as a category 3 study in the RMP in order to address MEA 86.2. This is a post-licensure observational study of the safety of Gardasil in males. The RMP version 14.1 has been updated. The MAH took the opportunity to update the RMP with the	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

protocol synopsis of the 2-dose effectiveness in Sweden (MEA 82.6 assessed by CHMP)." Opinion adopted on 09.04.2021.	
PRAC Led **Jinarc - tolvaptan - EMEA/H/C/002788/II/0029** Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Armando Genazzani, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "To update the RMP for Jinarc to version 14.4 to include dehydration and pregnancy prevention programme as requiring additional risk minimisation measures in accordance with Annex II." Opinion adopted on 09.04.2021. Request for Supplementary Information adopted on 14.01.2021, 29.10.2020, 11.06.2020.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Levemir - insulin detemir - EMEA/H/C/000528/II/0101** Novo Nordisk A/S, Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Kirstine Moll Harboe, "Update of sections 4.6 and 5.1 of the SmPC in order to update information on pregnancy, based on final results from the non-interventional Post-Authorisation Safety Study, NN304-4016, listed as a category 3 study in the RMP. This is a diabetes pregnancy registry study conducted to assess the long-term safety of insulin use in pregnant women. The RMP version 21.0 has also been submitted. The requested variation proposed amendments to the Summary of Product Characteristics and to the Risk Management Plan (RMP)." Opinion adopted on 09.04.2021. Request for Supplementary Information adopted on 11.02.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Nerlynx - neratinib - EMEA/H/C/004030/II/0020** Pierre Fabre Medicament, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 1.1 in order to add a new important identified risk, update data concerning the post authorisation safety studies and change of submission due date of the final Study Report of the PASS	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

n°6201 (MEA 001), from Q1 2021 to Q4 2021." Opinion adopted on 09.04.2021. Request for Supplementary Information adopted on 11.02.2021.	
PRAC Led **Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0024** Roche Registration GmbH, Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of section 4.4 of the SmPC to amend the wording on progressive multifocal leukoencephalopathy (PML) as requested in the conclusions of the latest periodic safety update report single assessment (PSUSA) procedure (PSUSA/00010662/202003) adopted in November 2020." Opinion adopted on 09.04.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Vimizim - elosulfase alfa - EMEA/H/C/002779/II/0034, Orphan** BioMarin International Limited, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of an updated RMP version 5.2 in order to update the safety specifications (epidemiology of indication and target populations, exposures in clinical trials and post marketing), the pharmacovigilance plan (routine and additional pharmacovigilance activities). Addition of an infusion reaction targeted questionnaire as routine pharmacovigilance activity. Deletion of a training material in section V.1 and addition of a process indicator to evaluate the distribution of the educational materials. The RMP has also been updated in line with EU RMP template (revision 2.0.1)." Opinion adopted on 09.04.2021. Request for Supplementary Information adopted on 14.01.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Zevalin - ibritumomab tiuxetan - EMEA/H/C/000547/II/0053** Ceft Biopharma s.r.o., Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Update of the RMP in line with the new GVP module" Request for Supplementary Information adopted on 09.04.2021.	Request for supplementary information adopted with a specific timetable.

PRAC Led **WS2009/G** **Edistride-EMEA/H/C/004161/WS2009/0045/G** **Forxiga-EMEA/H/C/002322/WS2009/0064/G** AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from studies MB102103, MB102104 and MB102110 listed as a category 3 study in the RMP. These are observational studies comparing the risk of severe complications of UTI, acute liver injury and acute kidney injury respectively, between patients with Type 2 Diabetes exposed to dapagliflozin and those exposed to other antidiabetic treatments. The RMP version 23.1 for Forxiga/Edistride has also been submitted. The requested grouped worksharing procedure proposed amendments to the Risk Management Plan (RMP)." Opinion adopted on 09.04.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS2011** **AZILECT-EMEA/H/C/000574/WS2011/0087** **Rasagiline ratiopharm-EMEA/H/C/003957/WS2011/0019** Teva B.V., Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Submission of an updated RMP (version 3.1) following the completion of study TV1030-CNS-50024 (listed as a category 3 study in the RMP): a non-interventional retrospective cohort study which was conducted using the United States Medicare research database to assess the potential risk of melanoma associated with the use of rasagiline mesylate in patients with Parkinson's disease (as assessed and concluded in procedure WS/1749 finalised in September 2020). The MAH took the opportunity to introduce a minor update to the targeted follow-up questionnaire for the important potential risk of malignant melanoma and to revise the list of safety concerns in line with GVP Module V revision 2.0.1" Opinion adopted on 09.04.2021. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 11.03.2021.	

B.5.5. CHMP-CAT assessed procedures

Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0021/G, ATMP CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder Opinion adopted on 22.04.2021, 16.04.2021. Request for Supplementary Information adopted on 19.02.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0022, ATMP CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, "Update of section 5.1 of the SmPC with the final results of study cod 16 HS 13, a 60-month follow up data assessing long-term efficacy and safety of Spherox. Annex II has also been updated to reflect the completion of the study. The requested variation proposed amendments to the Summary of Product Characteristics and Annex II." Opinion adopted on 22.04.2021, 16.04.2021. Request for Supplementary Information adopted on 19.03.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tecartus - autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - EMEA/H/C/005102/II/0001, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus Opinion adopted on 22.04.2021, 16.04.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0035, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus Opinion adopted on 22.04.2021, 16.04.2021.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zynteglo - betibeglogene autotemcel -	Request for supplementary information adopted

EMEA/H/C/003691/II/0022, Orphan, ATMP bluebird bio (Netherlands) B.V, Rapporteur: Carla Herberts, CHMP Coordinator: Paula Boudewina van Hennik Request for Supplementary Information adopted on 16.04.2021.	with a specific timetable.

B.5.6. CHMP-PRAC-CAT assessed procedures

Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0028, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, PRAC Rapporteur: Anette Kirstine Stark, "Update of section 4.8 of the SmPC on cytokine release syndrome (CRS) and neurologic adverse reaction grading and management and update of section 5.1 of the SmPC to include data from 36-month and 48-month analyses from ZUMA-1 study Cohorts 1 and 2. The Package leaflet is updated accordingly. In addition, other minor updates are included in the product information. The RMP (version 3.5) has been updated accordingly." Opinion adopted on 22.04.2021, 16.04.2021. Request for Supplementary Information adopted on 19.02.2021, 09.10.2020.	Positive Opinion adopted by consensus on 22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.7. PRAC assessed ATMP procedures

B.5.8. Unclassified procedures and worksharing procedures of type I variations

WS2003 **Silodyx-EMEA/H/C/001209/WS2003/0043** **Urorec-EMEA/H/C/001092/WS2003/0047** Recordati Ireland Ltd, Lead Rapporteur: Armando Genazzani Opinion adopted on 09.04.2021. Request for Supplementary Information adopted on 11.02.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2019 **Copalia-EMEA/H/C/000774/WS2019/0116** **Copalia HCT-EMEA/H/C/001159/WS2019/**	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

0091 **Dafiro-EMEA/H/C/000776/WS2019/0120** **Dafiro HCT-EMEA/H/C/001160/WS2019/0093** **Exforge-EMEA/H/C/000716/WS2019/0115** **Exforge HCT-EMEA/H/C/001068/WS2019/0090** Novartis Europharm Limited, Lead Rapporteur: Kirstine Moll Harboe Opinion adopted on 15.04.2021. Request for Supplementary Information adopted on 11.03.2021.	recommendation.
WS2022/G **Copalia-EMEA/H/C/000774/WS2022/0115/G** **Copalia HCT-EMEA/H/C/001159/WS2022/0089/G** **Dafiro-EMEA/H/C/000776/WS2022/0119/G** **Dafiro HCT-EMEA/H/C/001160/WS2022/0091/G** **Exforge-EMEA/H/C/000716/WS2022/0114/G** **Exforge HCT-EMEA/H/C/001068/WS2022/0088/G** Novartis Europharm Limited, Lead Rapporteur: Kirstine Moll Harboe, Opinion adopted on 15.04.2021. Request for Supplementary Information adopted on 11.03.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2025 **Hefiya-EMEA/H/C/004865/WS2025/0028** **Hyrimoz-EMEA/H/C/004320/WS2025/0028** Sandoz GmbH, Lead Rapporteur: Daniela Philadelphy Opinion adopted on 09.04.2021.	Positive Opinion adopted by consensus on 09.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2034 **Hexacima-EMEA/H/C/002702/WS2034/0115** **Hexyon-EMEA/H/C/002796/WS2034/0119** **MenQuadfi-EMEA/H/C/005084/WS2034/0002** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 15.04.2021.	Positive Opinion adopted by consensus on 15.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2041/G	Positive Opinion adopted by consensus on

Copalia-EMEA/H/C/000774/WS2041/0118/G **Dafiro-EMEA/H/C/000776/WS2041/0122/G** **Exforge-EMEA/H/C/000716/WS2041/0117/G** Novartis Europharm Limited, Lead Rapporteur: Kirstine Moll Harboe, Opinion adopted on 22.04.2021.	22.04.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.9. Information on withdrawn type II variation / WS procedure

Kaftrio - ivacaftor / tezacaftor / elexacaftor - EMEA/H/C/005269/II/0010, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 4.8 of the SmPC to introduce safety information related to liver failure based updated safety review of the company database. The PL is updated accordingly. The RMP of Kaftrio is updated" Withdrawal request submitted on 13.04.2021.	The MAH withdrew the procedure on 13.04.2021.
Rybelsus - semaglutide - EMEA/H/C/004953/II/0013 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Annika Folin, "Submission of the final study report for trial NN9535-4506 involving semaglutide s.c. and the updated RMP (version 6.0). The completed trial NN9535-4506 has been part of the additional pharmacovigilance activities as a category 3 study in the RMP for semaglutide to monitor the risk of neoplasms (malignant and non-malignant)." Withdrawal request submitted on 22.04.2021.	The MAH withdrew the procedure on 22.04.2021.

B.5.10. Information on type II variation / WS procedure with revised timetable

Remicade - infliximab - EMEA/H/C/000240/II/0227 Janssen Biologics B.V., Rapporteur: Kristina Dunder"Update of the breast-feeding information in section 4.6 of the SmPC to reflect the latest findings from literature regarding excretion of infliximab in human milk and the	Request by the applicant dated 15 April 2021 for an extension to the clock stop to respond to the request for supplementary information adopted in March 2021. The CHMP agreed to the request by the applicant.

lack of impact on the development of breastfed infants. The local representative section in the Package leaflet has also been updated."
Request for Supplementary Information adopted on 18.03.2021.

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

B.6.1. Start of procedure for New Applications: timetables for information

B.6.2. Start of procedure for Extension application according to Annex I of Reg. 1234/2008): timetables for information

B.6.3. Restart of procedure - responses received to Day 120 List of Questions timetables: for information

elivaldogene autotemcel -
EMEA/H/C/003690, Orphan
bluebird bio (Netherlands) B.V, treatment of ABCD1 genetic mutation and cerebral adrenoleukodystrophy
List of Outstanding Issues adopted on 16.04.2021.
List of Questions adopted on 22.01.2021.

B.6.4. Annual Re-assessments: timetables for adoption

Evoltra - clofarabine -
EMEA/H/C/000613/S/0072
Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant

Lamzede - velmanase alfa -
EMEA/H/C/003922/S/0019, Orphan
Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jan Neuhauser

B.6.5. Renewals of Marketing Authorisations: timetables for adoption provided only if the validation has been completed

Afstyla - lonoctocog alfa -
EMEA/H/C/004075/R/0037
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Johanna Lähteenvuo,

PRAC Rapporteur: Sonja Hrabcik

Darunavir Mylan - darunavir - EMEA/H/C/004068/R/0014
Mylan S.A.S, Generic, Generic of Prezista, Rapporteur: John Joseph Borg, PRAC Rapporteur: Liana Gross-Martirosyan

Emtricitabine/Tenofovir disoproxil Krka - emtricitabine / tenofovir disoproxil - EMEA/H/C/004215/R/0018
KRKA, d.d., Novo mesto, Generic, Generic of Truvada, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ana Sofia Diniz Martins

Emtricitabine/Tenofovir disoproxil Mylan - emtricitabine / tenofovir disoproxil - EMEA/H/C/004050/R/0016
Mylan S.A.S, Generic, Generic of Truvada, Rapporteur: Simona Stankeviciute, PRAC Rapporteur: Ana Sofia Diniz Martins

Fiasp - insulin aspart - EMEA/H/C/004046/R/0028
Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Annika Folin

Granpidam - sildenafil - EMEA/H/C/004289/R/0009
Accord Healthcare S.L.U., Generic, Generic of Revatio, Rapporteur: Kolbeinn Gudmundsson, PRAC Rapporteur: Menno van der Elst

Movymia - teriparatide - EMEA/H/C/004368/R/0024
STADA Arzneimittel AG, Duplicate, Duplicate of Terrosa, Rapporteur: Daniela Philadelphy, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ronan Grimes

Olumiant - baricitinib - EMEA/H/C/004085/R/0025
Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Christophe Focke, PRAC Rapporteur: Adam Przybylkowski

Parsabiv - etelcalcetide - EMEA/H/C/003995/R/0017
Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Andrea Laslop (AT) (MNAT with AT for Clinical Efficacy, AT for Clinical Safety, AT for Non-Clinical, AT for Clinical Pharmacology, AT for Coordination, DE-

BfArM for Quality), PRAC Rapporteur: Ilaria Baldelli

SomaKit TOC - edotreotide - EMEA/H/C/004140/R/0019, Orphan
Advanced Accelerator Applications, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Ronan Grimes

Tenofovir disoproxil Mylan - tenofovir disoproxil - EMEA/H/C/004049/R/0022
Mylan S.A.S, Generic, Generic of Viread, Rapporteur: Simona Stankeviciute, PRAC Rapporteur: Adrien Inoubli

Terrosa - teriparatide - EMEA/H/C/003916/R/0020
Gedeon Richter Plc., Rapporteur: Daniela Philadelphy, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ronan Grimes

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

B.6.7. Type II Variations scope of the Variations: Extension of indication

Briviact - brivaracetam - EMEA/H/C/003898/II/0032/G
UCB Pharma S.A., Rapporteur: Filip Josephson, PRAC Rapporteur: Adam Przybylkowski, "- Extension of indication to include patients from 1 month to 4 years of age for the Briviact treatment; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The RMP version 8.0 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.2 and the MAH took the opportunity to implement minor editorial updates.
- (B.II.f.1.b.2)
- (B.IV.1.a.1)
The Package Leaflet and Labelling are updated in accordance."

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0104
Merck Sharp & Dohme B.V., Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "Extension of indication for Keytruda to include in combination with lenvatinib first-line

treatment of adults with advanced renal cell carcinoma (RCC); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 32.1 of the RMP has also been submitted."

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0105

Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst, "Extension of indication to include pembrolizumab in combination with lenvatinib for the treatment of advanced endometrial carcinoma in adults who have disease progression following prior systemic therapy in any setting and who are not candidates for curative surgery or radiation; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 33.1 of the RMP has also been submitted."

Kisplyx - lenvatinib - EMEA/H/C/004224/II/0045

Eisai GmbH, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: David Olsen, "Extension of indication for Kisplyx to include in combination with pembrolizumab first-line treatment of adults with advanced renal cell carcinoma (RCC); as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 13 of the RMP has also been submitted. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet."

Lenvima - lenvatinib - EMEA/H/C/003727/II/0042

Eisai GmbH, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Annika Folin, "Extension of indication to include lenvatinib in combination with pembrolizumab for the treatment of adult patients with advanced endometrial carcinoma (EC) who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation; as a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.

Version 14.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to make minor editorial changes to the SmPC and update the list of local representatives in the Package Leaflet in line with the latest QRD template version 10.2." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
OPDIVO - nivolumab - EMEA/H/C/003985/II/0100 Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of indication for Opdivo to include adjuvant treatment of adults with muscle invasive urothelial carcinoma (MIUC) who are at high risk of recurrence after undergoing radical resection of MIUC; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 23.0 of the RMP has also been submitted."	
Repatha - evolocumab - EMEA/H/C/003766/II/0049/G Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Kimmo Jaakkola, "C.I.6 (EoI) Extension of indication to include one new paediatric indication in paediatric patients aged 10 years and over with heterozygous familial hypercholesterolaemia as an adjunct to diet, alone or in combination with other lipid-lowering therapy, to reduce LDL-C based on results of study 20120123 (HAUSER-RCT). It is a randomized, multicenter, placebo-controlled, double blind, parallel group, 24 week trial in 158 paediatric patients aged 10 to > 18 years with heterozygous familial hypercholesterolaemia. As a consequence, sections 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet are updated in accordance. Version 7.0 of the RMP has also been submitted. C.I.6 (EoI) Extension of indications to modify the existing indication for treatment of adults and paediatric patients aged 10 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies based on interim results from study 20120124	

(HAUSER-OLE). It was an open label, single arm, multicenter, 80 week trial to evaluate the safety, tolerability and efficacy of Repatha for LDL-C reduction in paediatric patients from aged ≥ 10 to < 18 years of age with homozygous familial hypercholesterolaemia. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated accordingly."

Skyrizi - risankizumab - EMEA/H/C/004759/II/0014

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely, PRAC Rapporteur: Liana Gross-Martirosyan, "Extension of indication for the treatment of active psoriatic arthritis in adults. Consequently sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 to the SmPC have been updated. The Package leaflet is updated accordingly. Additionally, Annex II is also updated."

Zepatier - elbasvir / grazoprevir - EMEA/H/C/004126/II/0029

Merck Sharp & Dohme B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ana Sofia Diniz Martins, "Extension of indication to include treatment of chronic hepatitis C (CHC) in paediatric patients 12 years of age and older who weigh at least 30 kg for Zepatier; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

WS2049/G
Lacosamide UCB-EMEA/H/C/005243/ WS2049/0009/G
Vimpat-EMEA/H/C/000863/WS2049/ 0091/G

UCB Pharma S.A., Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ulla Wändel Liminga, "Extension of indication to include patients from 1 month to 4 years of age for treatment of partial-onset seizures with or without secondary generalisation as monotherapy and adjunctive therapy for Vimpat/Lacosamide USB. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC

are updated. Version 16.0 of the RMP has also been submitted. B.IV.1.a.1 - B.II.f.1.b.2 - The Package Leaflet and labelling are updated in accordance.”	

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0021/G Baxalta Innovations GmbH, Rapporteur: Andrea Laslop	
Bemfola - follitropin alfa - EMEA/H/C/002615/II/0029 Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik	
Benlysta - belimumab - EMEA/H/C/002015/II/0094 GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder	
Bridion - sugammadex - EMEA/H/C/000885/II/0041/G Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola	
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0022/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 21.04.2021. Request for Supplementary Information adopted on 14.04.2021.	See also B.5.1
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0026 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 21.04.2021.	See also B.5.1
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0027 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COVID-19 Vaccine Moderna - COVID-19	

mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0011/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 22.04.2021.	See also B.5.1
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0128 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0106/G Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0107 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani	
Nimenrix - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0108/G Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad	
Ontruzant - trastuzumab - EMEA/H/C/004323/II/0032 Samsung Bioepis NL B.V., Rapporteur: Karin Janssen van Doorn	
Palynziq - pegvaliase - EMEA/H/C/004744/II/0019, Orphan BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege	
Remsima - infliximab - EMEA/H/C/002576/II/0101/G Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola	
Replagal - agalsidase alfa - EMEA/H/C/000369/II/0112/G Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege	
Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0053/G CSL Behring GmbH, Rapporteur: Kristina Dunder	
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus	

type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0077
MCM Vaccine B.V., Rapporteur: Christophe Focke

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0079
MCM Vaccine B.V., Rapporteur: Christophe Focke

Xofigo - radium-223 - EMEA/H/C/002653/II/0041
Bayer AG, Rapporteur: Janet Koenig

Xofigo - radium-223 - EMEA/H/C/002653/II/0042/G
Bayer AG, Rapporteur: Janet Koenig

Zirabev - bevacizumab - EMEA/H/C/004697/II/0019
Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad

WS1908/G
Hefiya-EMEA/H/C/004865/WS1908/0030/G
Hyrimoz-EMEA/H/C/004320/WS1908/0030/G
Sandoz GmbH, Lead Rapporteur: Daniela Philadelphy

WS2062
M-M-RVAXPRO-EMEA/H/C/000604/WS2062/0106
ProQuad-EMEA/H/C/000622/WS2062/0146
MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus

WS2068/G
Blitzima-EMEA/H/C/004723/WS2068/0042/G
Ritemvia-EMEA/H/C/004725/WS2068/0042/G
Truxima-EMEA/H/C/004112/WS2068/0045/G
Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz

B.6.9. CHMP assessed procedures scope: Non-Clinical and Clinical aspects

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0098

UCB Pharma S.A., Rapporteur: Kristina Dunder, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information on reduction of anterior uveitis flares in patients diagnosed with active axial spondyloarthritis based on the final results from study AS0007 (C-VIEW); this is a multicenter, open-label study to assess the effects of certolizumab pegol on the reduction of anterior uveitis flares in axial spondyloarthritis subjects with a history of anterior uveitis."

COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0023/G

BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson

Dapivirine Vaginal Ring 25 mg - dapivirine - EMEA/H/W/002168/II/0007

International Partnership for Microbicides Belgium AISBL, Rapporteur: Paula Boudewina van Hennik, "Submission of the final report for study report no. 15760.01, conducted to evaluate the antiviral activity of dapivirine on hepatitis E virus (HEV) in vitro. In addition, the SOH took the opportunity to submit data on: antiviral activity of Dapivirine against influenza A and B viruses; the effects of a vaginal film formulation of dapivirine on various species of Lactobacilli present in the vagina; the antitumor activity of dapivirine in glioblastoma cells. With this submission, the post authorisation measure REC 001 is addressed."

Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0018

Sanofi Pasteur, Rapporteur: Christophe Focke, "Submission of the final report from study DNG10042, listed as a category 3 study in the RMP. This report summarises the findings on the dengue vaccine (Dengvaxia) effectiveness against virologically confirmed symptomatic infection, carried out after the mass vaccination program conducted by the Brazilian state of Paraná from 2016 to 2018."

Entyvio - vedolizumab -

EMEA/H/C/002782/II/0059/G
Takeda Pharma A/S, Rapporteur: Armando Genazzani, "C.I.4
Update of section 4.6 of the SmPC in order to implement information on lactation based on study Vedolizumab-4001 (An Open-Label, Multicenter and Open Enrollment Model, Postmarketing, Milk-Only Lactation Study to Assess Concentration of Vedolizumab in Breast Milk of Lactating Women With Active Ulcerative Colitis or Crohn's Disease Who Are Receiving Vedolizumab Therapeutically). The study aimed to determine the PK parameters of vedolizumab in breast milk and to estimate mean daily infant dosage over the dosing interval through breast milk, and percentage of maternal dose consumed in breast milk by the infants.
C.I.4
Update of section 5.2 of the SmPC in order to adjust the values for clearance and serum half-life of vedolizumab IV and SC in subjects with ulcerative colitis and Crohn's disease. The updated pop PK dataset consists of pooled data across 4 phase 3 studies (C13006, C13007, MLN0002SC-3027, MLN0002SC-3031) and 1 open-label extension study (MLN0002SC-3030). In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to correct minor typographical errors and to bring the PI in line with the latest QRD template version 10.2 rev. 1."

Jinarc - tolvaptan -
EMEA/H/C/002788/II/0033/G
Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Armando Genazzani, "Update of section 4.5 of the SmPC in order to update the safety information based on final results from study 156-201-00233 and 156-201-00234; the Package Leaflet is updated accordingly."

Kisqali - ribociclib -
EMEA/H/C/004213/II/0028
Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 5.3 of the SmPC in order to update non-clinical information based on results from a 2-year carcinogenicity study in rats"

Lynparza - olaparib -
EMEA/H/C/003726/II/0047
AstraZeneca AB, Rapporteur: Alexandre Moreau,

"Update of sections 4.8 and 5.1 of the SmPC in order to update safety and efficacy information based on the final analysis of overall survival and safety update from study POLO, a Phase III, randomised, double-blind, placebo-controlled, multicentre study in gBRCAm patients with metastatic pancreatic adenocarcinoma whose disease had not progressed after receiving first-line platinum-based chemotherapy."	
Oncaspar - pegaspargase - EMEA/H/C/003789/II/0038 Les Laboratoires Servier, Rapporteur: Alexandre Moreau, "Update of sections 4.4 and 4.8, of the SmPC in order to add a new warning on the risk of osteonecrosis and to include it as an adverse drug reaction associated with pegaspargase use with an unknown frequency, following review of all available non-clinical, epidemiological and clinical data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2."	
Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0032 Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to add new information on efficacy and safety based on final results from study GS-US-320-4035. This was a phase 2, open-label study to evaluate the safety and efficacy of switching to tenofovir alafenamide from tenofovir disoproxil fumarate and/or other oral antiviral treatment in virologically suppressed chronic hepatitis B subjects with renal and/or hepatic impairment."	
Votrient - pazopanib - EMEA/H/C/001141/II/0067/G Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, "C.I.4 Update of section 4.8 of the SmPC in order to add hepatic failure to the list of adverse drug reactions (ADRs) with frequency not known, the Package Leaflet is updated accordingly. C.I.4 Update of section 4.4 of the SmPC in order to update the description of "Combination with other systemic anti-cancer therapies' to simplify and to include the known studies with anti-	

cancer agents that were terminated early (pemetrexed, lapatinib and more recently also pembrolizumab). Type IA A.6 update the SmPC with the updated ATC codes released by WHO.”	
ZABDENO - ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337/II/0003 Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 and 4.8 of the SmPC to add a new warning on febrile seizures in children and to include "febrile seizures" on the list of adverse drug reactions (ADRs) with frequency rare, based on the review of febrile seizures post-marketing cases received within the GMS Global Safety Database. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to replace the local representative for the UK with a local representative for the territory of Northern Ireland as a consequence of the Northern Ireland Protocol.”	
WS2008/G **Mekinist-EMEA/H/C/002643/WS2008/0046/G** **Tafinlar-EMEA/H/C/002604/WS2008/0051/G** Novartis Europharm Limited, Lead Rapporteur: Paula Boudewina van Hennik, “C.I.4 Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 5-years efficacy results from Phase III study COMBI-AD. This is a two-arm, randomized, double-blind Phase III study of dabrafenib in combination with trametinib versus two placebos in the adjuvant treatment of melanoma after surgical resection in adult patients with a BRAF V600 mutation. Type IA A.6 update the SmPC with the updated ATC codes released by WHO”	
WS2039 **Genvoya-EMEA/H/C/004042/WS2039/0076** **Stribild-EMEA/H/C/002574/WS2039/0116** **Tybost-EMEA/H/C/002572/WS2039/0058** Gilead Sciences Ireland UC, Lead Rapporteur: Bruno Sepodes, “Update of section 4.5 of the SmPC to add new information about the drug-	

drug interactions between cobicistat containing products (Genvoya, Tybost and Stribild) and corticosteroids, based on post-marketing data. Furthermore, the MAH took the opportunity to bring the Tybost Product Information in line with version 10.2 of the QRD template and update the list of local representatives. Moreover, minor editorial updates and corrections have been introduced throughout the Product Information of all three products."

WS2052/G
Stayveer-EMEA/H/C/002644/WS2052/0034/G
Tracleer-EMEA/H/C/000401/WS2052/0099/G
Janssen-Cilag International NV, Lead Rapporteur: Alexandre Moreau, "
Grouped variation application;

- Type II variation, C.I.4: Update of section 4.6 of the SmPC to correct the information related to male fertility based on a review of study AC-052-402 carried out by the MAH.
- Type IA variation, A.7

In addition, the WSA took the opportunity to update the list of local representatives in the Package Leaflet. The WSA also took the opportunity to correct some errors in the national translations."

WS2054
Enerzair Breezhaler-EMEA/H/C/005061/WS2054/0003
Zimbus Breezhaler-EMEA/H/C/005518/WS2054/0003
Novartis Europharm Limited, Lead Rapporteur: Peter Kiely, "Update of section 5.1.Pharmacodynamic properties, based on the final results from the ARGON study a Phase 3b, multicenter, partially-blinded, randomized, 24-week, parallel-group, non-inferiority, open-label active controlled study comparing the efficacy and safety of QVM149 with a free triple combination of salmeterol/fluticasone + tiotropium in patients with uncontrolled asthma."

WS2066
Lacosamide UCB-EMEA/H/C/005243/WS2066/0010
Vimpat-EMEA/H/C/000863/WS2066/0092
UCB Pharma S.A., Lead Rapporteur: Filip

Josephson, "Update of section 4.8 of the SmPC in order to add Dyskinesia to the list of adverse drug reactions (ADRs) with frequency uncommon following the outcome of continuous safety signal assessments of the relevant reported clinical and post-marketing cases. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the PI and to bring it in line with the latest QRD template version 10.2 and relevant guidelines."

B.6.10. CHMP-PRAC assessed procedures

BYETTA - exenatide - EMEA/H/C/000698/II/0075 AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of sections 4.2 and 5.1 of the SmPC based on the results of study H8O-MC-GWBQ (assessed by CHMP as part of PAM P46 048); a 28-week, randomised, double-blind, placebo-controlled study to evaluate the safety and efficacy of exenatide twice daily in 120 patients aged 10 to 17 years, and study 2993-124; a randomised, single-blind, placebo-controlled, dose-rising study to evaluate the PK, PD and tolerability of exenatide in adolescent patients). The RMP version 35.1 has also been submitted."
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0055 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, "Submission of a final Clinical Study Report of study MO28231 (KAMILLA) and fulfil a category 3 Additional Pharmacovigilance Activity in the Risk Management Plan to address the following safety concerns: Ventricular Dysfunction, Safety in Elderly Patients and the Use of a non-validated HER2 test. The updated RMP (version 13) is submitted to remove the commitment for this study and the safety concern "use of non-validated HER2 test"."
Mavenclad - cladribine - EMEA/H/C/004230/II/0020 Merck Europe B.V., Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "C.I.4 Type II Update of

sections 4.2 and 4.4 of the SmPC in order to change posology recommendations by adding an advice on preventive measures to avoid liver injury and to add a new warning on liver function and liver injury based on a review of post-approval data in MAH's safety database, non-clinical and clinical trial data and scientific literature (cladribine and liver injury and epidemiological data on hepatic injury in MS). The Package Leaflet is updated accordingly. The RMP version 1.6 has also been submitted."	
Rybelsus - semaglutide - EMEA/H/C/004953/II/0013 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Annika Folin, "Submission of the final study report for trial NN9535-4506 involving semaglutide s.c. and the updated RMP (version 6.0). The completed trial NN9535-4506 has been part of the additional pharmacovigilance activities as a category 3 study in the RMP for semaglutide to monitor the risk of neoplasms (malignant and non-malignant)."	
Tremfya - guselkumab - EMEA/H/C/004271/II/0028 Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, "C.I.4 Update of sections 4.8 and 5.1 of the SmPC in order to update the EU product information with 5 years data from the final study reports of pivotal psoriasis studies PSO3001 and PSO3002 listed as additional PV activities (category 3 studies) in the RMP; in the long term extension part of these studies subjects received open-label guselkumab q8w, starting at Week 52 in PSO3001 and at Week 76 in PSO3002, with the last dose at Week 252 and the last safety follow-up visit at Week 264. The RMP version 8.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."	
WS2069/G Edistride-EMEA/H/C/004161/WS2069/0048/G Forxiga-EMEA/H/C/002322/WS2069/0067/G AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin,	

"Grouped submission of final study reports of the DETERMINE studies D169EC00001 and D169EC00002, listed as category 3 PASS studies, assessing the risk of lower limb amputation. Both studies are international, multicentre, parallel-group, randomised, double-blind, placebo-controlled, Phase III Study evaluating the effect of Dapagliflozin on Exercise capacity: study D169EC00001 in patients with heart failure with preserved ejection fraction (HFpEF); study D169EC00002 in patients with heart failure with reduced ejection fraction (HFrEF). The RMP version 25 has also been submitted. The studies are proposed to be removed from the Post-Authorisation Development Plan in the RMP for Forxiga and Edistride."	

B.6.11. PRAC assessed procedures

PRAC Led **Beovu - brolucizumab - EMEA/H/C/004913/II/0008** Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to include the description of intraocular inflammation, based on final results from a non-interventional retrospective real-world evidence study conducted in patients with neovascular (wet) age-related macular degeneration (nAMD) to better understand the incidence of adverse events/safety signal after initiating treatment with brolucizumab for up to 6 months."	
PRAC Led **Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0099** UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study (RA0020) listed as a category 3 study in the RMP. This is a nationwide prospective observational cohort study in Germany on the long-term safety and effectiveness of bDMARDs in rheumatoid arthritis (RA). In addition, this submission	

includes a safety analysis across the 4 completed RA registries (ARTIS, NDB, BSRBR and RABBIT) as requested by EMA/PRAC in the final assessment report of Procedures EMEA/H/C/001037/II/0072, EMEA/H/C/001037/II/0081, and EMA/H/C/001037/II/0087. Based on this, revisions to the RMP summary of safety concerns and consequently the pharmacovigilance plan are proposed in line with GVP Module V Rev.2. An updated RMP v19.0 is included."

PRAC Led

Dacogen - decitabine - EMEA/H/C/002221/II/0044, Orphan

Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Update of section 4.6 of the SmPC in order to update information on fertility, pregnancy and lactation, following PSUR procedure PSUSA/00009118/202005; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives for Italy in the Package Leaflet and to include some editorial changes in the PI to align with standard English spelling."

PRAC Led

Faslodex - fulvestrant - EMEA/H/C/000540/II/0073

AstraZeneca AB, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Filip Josephson, "Update of the RMP version 13 for fulvestrant to remove the additional risk minimisation measures for important identified risks and reclassifiy safety concerns based on Good Pharmacovigilance Practices (GVP) module V, risk management systems (revision 2) guidelines as requested by PRAC as a part of PRAC PSUR assessment report, procedure number EMEA/H/C/PSUSA/00001489/202004 covering the period 26/04/2017 to 25/04/2020."

PRAC Led

HyQvia - human normal immunoglobulin - EMEA/H/C/002491/II/0070/G

Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan

Mueller-Berghaus, "C.I.4 (Type II) - Update of section 4.6 of the SmPC in order to update information on pregnancy and breast-feeding based on the final results from study 161301 listed as a category 3 study in the RMP; this is an observational study to collect long-term safety data from women treated with HyQvia. The package leaflet has been updated accordingly. RMP version 12.0 has also been submitted. In addition, the MAH took the opportunity to implement minor corrections and editorial changes to the SmPC. C.I.11.b (Type II) – Submission of an updated RMP version 12.0 to update the educational material section Part V.2, additional Risk Minimisation Measures, for HyQvia. The change was requested by the PRAC in the outcome of the PSUSA procedure EMEA/H/C/PSUSA/00001633/202005. "	
PRAC Led **InductOs - dibotermin alfa - EMEA/H/C/000408/II/0100** Medtronic BioPharma B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Pieter de Graeff, "C.I.11.b - Submission of an updated RMP version 2.1 in order to submit the final study report from study EUPAS32916 listed as category 3 study in the RMP. This is an observational study to evaluate the effectiveness of additional Risk Minimisation Measures for InductOs. In addition, the MAH took the opportunity to submit study protocol for study EUPAS32916 that was agreed by PRAC."	
PRAC Led **Lojuxta - lomitapide - EMEA/H/C/002578/II/0047** Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "To introduce an enhanced pharmacovigilance system to evaluate the occurrence and outcomes of pregnancy in females of reproductive potential treated with lomitapide who decide to continue the pregnancy following advice from a teratologist/clinician, replacing the currently agreed Pregnancy Exposure Register (PER), which is listed as part of the specific obligations	

in the Annex II. The RMP version 6.5 has also been submitted. In addition, the MAH took the opportunity to introduce minor administrative changes."

PRAC Led

Norvir - ritonavir - EMEA/H/C/000127/II/0161

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 7.1 in order to comply with revision 2 of the template. In addition, the MAH reviewed the information contained in the Norvir RMP and made the following updates:
-Removal of important identified risk of toxicity of Norvir oral solution in preterm neonates.
-Removal of missing information regarding use of ritonavir in elderly patients.
-Analysis of the Antiretroviral Pregnancy Registry (APR) data will be provided with the ritonavir PSUR."

PRAC Led

Orphacol - cholic acid - EMEA/H/C/001250/II/0040, Orphan

Laboratoires CTRS, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Sofia Trantza, PRAC-CHMP liaison: Konstantinos Markopoulos, "Submission of an updated RMP version 4.0 in order to reflect the current status of the additional risk minimisation measures. Furthermore, the format of the RMP was adapted to the new template and protocol of the patient for the ongoing patient surveillance database study was included as approved in May 2020 in an Art107o procedure."

PRAC Led

Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0126/G

Boehringer Ingelheim International GmbH, Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Kirstine Moll Harboe, "C.I.13: Submission of the final report from drug utilisation study, 1160.129, GLORIA AF. This is a three-phase, international, multicenter, prospective, observational registry program in patients with newly diagnosed non-valvular

atrial fibrillation (NV AF) at risk for stroke. The objective of the registry program is to investigate patient characteristics influencing the choice of antithrombotic treatment for the prevention of stroke in NV AF patients globally and to collect data from clinical practice settings on important outcome events of antithrombotic treatments for the prevention of stroke.
C.I.13: Submission of the final report from drug utilisation study, 1160.136, EU GLORIA AF listed as a category 3 study in the RMP. This is a three-phase, international, multicenter, prospective, observational registry program in patients with newly diagnosed non-valvular atrial fibrillation (NV AF) at risk for stroke. The objective of the registry program is to investigate patient characteristics influencing the choice of antithrombotic treatment for the prevention of stroke in NV AF patients from participating countries in EU/EEA Member States and to collect data from clinical practice settings on important outcome events of antithrombotic treatments for the prevention of stroke. The RMP version 39 has also been submitted."

PRAC Led

Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0045

GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke, PRAC Rapporteur: Sonja Hrabcik, PRAC-CHMP liaison: Andrea Laslop, "Update of section 4.4 of the SmPC in order to add a new warning on an increased risk of Guillain-Barré Syndrome (GBS) after vaccination with Shingrix observed in a post-marketing observational study in individuals aged 65 years or older. The RMP version 5.1 has also been submitted. In addition, the MAH took the opportunity to make some editorial changes to the SmPC and to update the list of local representatives in the Package Leaflet."

PRAC Led

Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0014

AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Christophe Focke, "Update of sections 4.3, 4.4 and 4.8 of the SmPC, following an update to the Company Core Data Sheet in

relation to thromboembolism with thrombocytopenia, to contraindicate the vaccine to patients who have experienced major venous and/or arterial thrombosis in combination with thrombocytopenia following vaccination with any COVID-19 vaccine, update the warnings on thrombocytopenia and coagulation disorders and include the frequency thrombosis with thrombocytopenia of "less than 1/100,000". The package leaflet is updated accordingly."

PRAC Led
WS2043
OPDIVO-EMEA/H/C/003985/WS2043/0102
Yervoy-EMEA/H/C/002213/WS2043/0087
Bristol-Myers Squibb Pharma EEIG, Lead PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "To provide an updated RMP to change the final due date for the PAES Study CA2098Y8 (a Phase 3b, Randomized, Double-blind Study of Nivolumab Combined with Ipilimumab versus Nivolumab Monotherapy for Patients with Previously Untreated Advanced Renal Cell Carcinoma and Intermediate- or Poor-Risk Factors).
In addition, the marketing authorisation holder has taken the opportunity to include a minor editorial revision in the French translation of the PI as previously agreed with the Agency. "

PRAC Led
WS2057
Aerius-EMEA/H/C/000313/WS2057/0098
Azomyr-EMEA/H/C/000310/WS2057/0102
Neoclarityn-EMEA/H/C/000314/WS2057/0096
Organon N.V., Duplicate, Duplicate of Allex (SRD), Azomyr, Opulis (SRD), Lead Rapporteur: Christophe Focke, Lead PRAC Rapporteur: Laurence de Fays, PRAC-CHMP liaison: Karin Janssen van Doorn, "Submission of an updated RMP version 2.1 in order to align with GVP Module V (rev 2) template which includes updates to the list of safety concerns and reflects the completion of a post-authorisation safety study listed as category 3 (A Nordic register-based study which studied the association between the use of desloratadine and risk of seizures, supraventricular tachycardia, and atrial fibrillation or flutter:

EUPAS15038) assessed in EMEA/H/WS1655."

PRAC Led

WS2064

Nuwiq-EMEA/H/C/002813/WS2064/0043

Vihuma-EMEA/H/C/004459/WS2064/0024

Octapharma AB, Lead PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "To provide an updated RMP to remove the completed studies GENA-05 and GENA-15. As a consequence, in the section 'Missing Information' the following safety concerns have been removed: "Safety in previously untreated patients", "Children < 2 years" and "Immune tolerance induction". No new safety concerns were added. In addition, the RMP has been updated to GVP Module V Rev.2."

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

B.6.15. Unclassified procedures and worksharing procedures of type I variations

WS2002

Filgrastim Hexal-EMEA/H/C/000918/WS2002/0061

Zarzio-EMEA/H/C/000917/WS2002/0062

Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege

WS2042

Ambirix-EMEA/H/C/000426/WS2042/0115

Fendrix-EMEA/H/C/000550/WS2042/0075

Infanrix hexa-EMEA/H/C/000296/WS2042/0298

Twinrix Adult-EMEA/H/C/000112/WS2042/0150

Twinrix Paediatric-EMEA/H/C/000129/WS2042/0151

GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

WS2055

Actraphane-EMEA/H/C/000427/WS2055/0089 **Actrapid-EMEA/H/C/000424/WS2055/0083** **Insulatard-EMEA/H/C/000441/WS2055/0087** **Mixtard-EMEA/H/C/000428/WS2055/0090** **Protaphane-EMEA/H/C/000442/WS2055/0086** Novo Nordisk A/S, Lead Rapporteur: Kirstine Moll Harboe	
WS2056 **Fiasp-EMEA/H/C/004046/WS2056/0029** **NovoMix-EMEA/H/C/000308/WS2056/0108** **NovoRapid-EMEA/H/C/000258/WS2056/0140** Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder	
WS2060 **HyQvia-EMEA/H/C/002491/WS2060/0071** **Kiovig-EMEA/H/C/000628/WS2060/0109** Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus	
WS2061/G **Rixathon-EMEA/H/C/003903/WS2061/0048/G** **Riximyo-EMEA/H/C/004729/WS2061/0048/G** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, "B.II.f.1.d - C.I.2.a - To update section 4 of the Package Leaflet to add the side effect 'tumour pain' from the 1400 mg/ml and 1600 mg/ml strength (both subcutaneously administered) to the 100 mg/ml and 500 mg/ml (both intravenously administered) and to update of the statement on sodium in section 2 of the package leaflet in line with the EC guideline Excipients in the labelling and package leaflet of medicinal products for human use (EMA/CHMP/302620/2017 Rev 1) following assessment of the same change for reference product Mabthera (EMEA/H/C/000165/II/0177). Furthermore, the MAH took the opportunity to introduce minor editorial corrections product information as listed in the present and proposed table."	

WS2063
Ryzodeg-EMEA/H/C/002499/WS2063/
0046
Tresiba-EMEA/H/C/002498/WS2063/0052
Xultophy-EMEA/H/C/002647/WS2063/
0041
Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder

B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY

B.7.1. Yearly Line listing for Type I and II variations

B.7.2. Monthly Line listing for Type I variations

B.7.3. Opinion on Marketing Authorisation transfer (MMD only)

B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only)

B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only)

B.7.6. Notifications of Type I Variations (MMD only)

C. Annex C - Post-Authorisation Measures (PAMs), (Line listing of Post authorisation measures with a description of the PAM. Procedures starting in that given month with assessment timetabled)

D. Annex D - Post-Authorisation Measures (PAMs), (Details on PAMs including description and conclusion, for adoption by CHMP in that given month, or finalised ones with PRAC recommendation and no adoption by CHMP needed)

E. Annex E - EMA CERTIFICATION OF PLASMA MASTER FILES

Information related to plasma master files cannot be released at the present time as these contain commercially confidential information.

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

F. ANNEX F - Decision of the Granting of a Fee Reduction/Fee Waiver

G. ANNEX G

G.1. Final Scientific Advice (Reports and Scientific Advice letters)

G.2. PRIME

Some information related to PRIME cannot be released at the present time as these contain commercially confidential information.

G.2.1. List of procedures concluding at 19-22 April 2021 CHMP plenary:

Psychiatry	
Treatment of cognitive impairment in adult patients with schizophrenia (CIAS)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Haematology – Hemostaseology	
CTX001, ATMP, Treatment of transfusion-dependent β-thalassemia	The CHMP granted eligibility to PRIME and adopted the critical summary report.
Gastroenterology-Hepatology	
Treatment of Primary Biliary Cholangitis	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Oncology	
Treatment of Glioblastoma	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Endocrinology-Gynaecology-Fertility-Metabolism	
Delay of preterm delivery in women with spontaneous preterm labour	The CHMP denied eligibility to PRIME and adopted the critical summary report.

G.2.2. List of procedures starting in April 2021 for May 2021 CHMP adoption of outcomes

H. ANNEX H - Product Shared Mailboxes – e-mail address